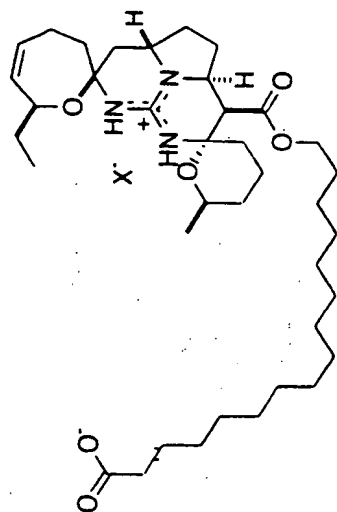
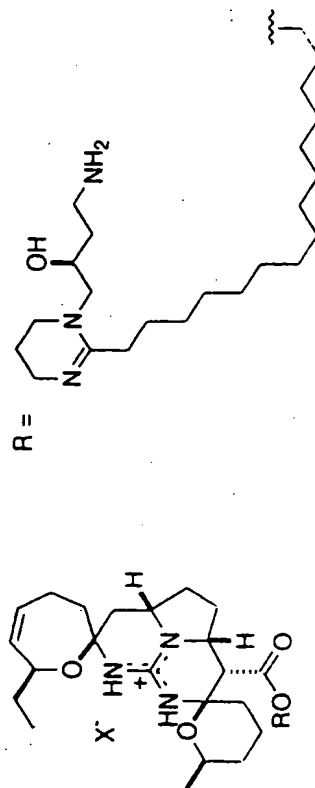


pilomycin A (1, $R^1 = R^2 = R^3 = H$; $n = 1$)
 crambescidin 800 (2, $R^1 = R^3 = H$, $R^2 = OH$; $n = 1$)
 crambescidin 816 (3, $R^1 = R^2 = OH$, $R^3 = H$; $n = 1$)
 crambescidin 830 (4, $R^1 = R^2 = OH$, $R^3 = H$; $n = 2$)
 crambescidin 844 (5, $R^1 = R^2 = OH$, $R^3 = H$; $n = 3$)
 celeromycin (6, $R^1 = R^2 = H$, $R^3 = OH$; $n = 1$)

13, 14, 15 - isocrambescidin 800 (10)



13, 14, 15 - isocrambescidin 657 (10a)



fromiamycin (9)

$R = H$ (7)
 $R = allyl$ (8)

Figure 1

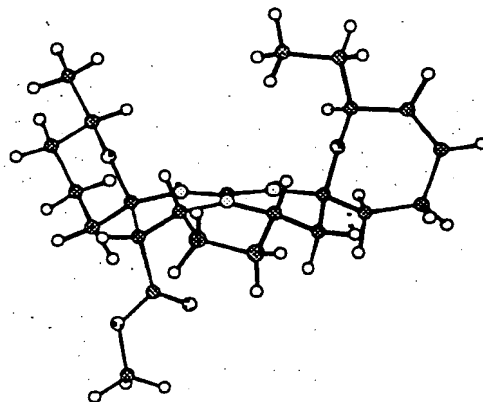


Figure 2

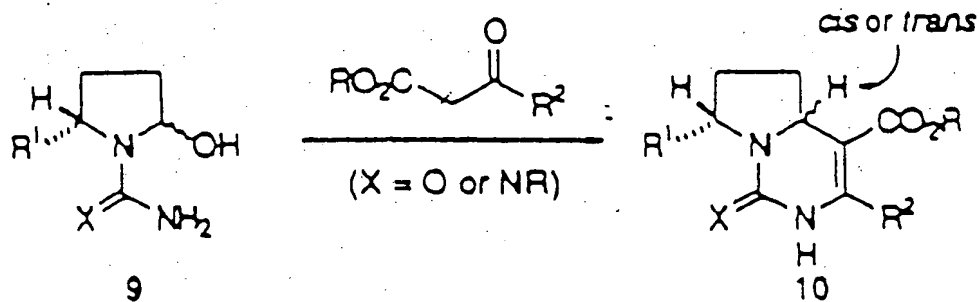
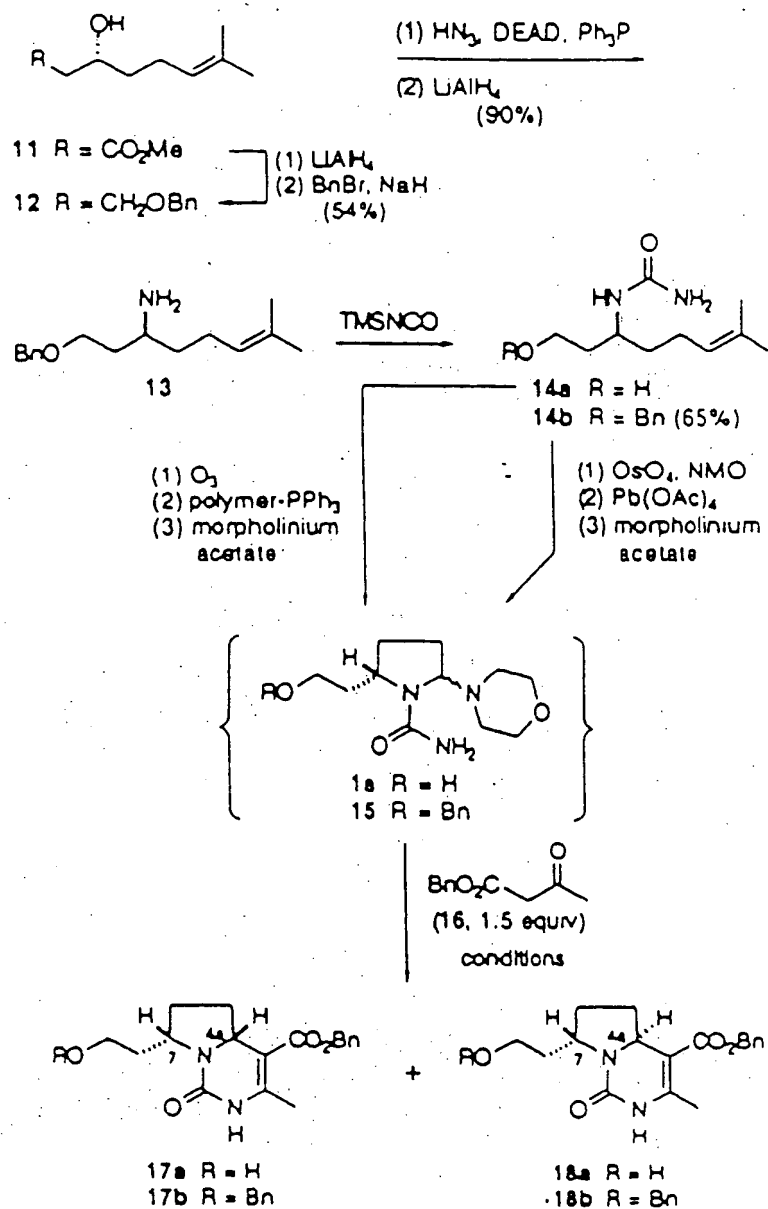


FIGURE . 3



| substrate | reaction conditions | 17:18 (yield) ^a |
|-----------|-----------------------------------------------------------------------------------|----------------------------|
| 1a | morpholinium acetate (1.5 eq), $\text{CF}_3\text{CH}_2\text{OH}$, 60 °C, 48 h | 4:1 (80%) |
| 15 | | 4:1 (81%) |
| 15 | PPE, CH_2Cl_2 , 23 °C, 48 h | 1:4 (60%) |

^a Combined overall yield of 17 and 18 from 14.

FIGURE 4

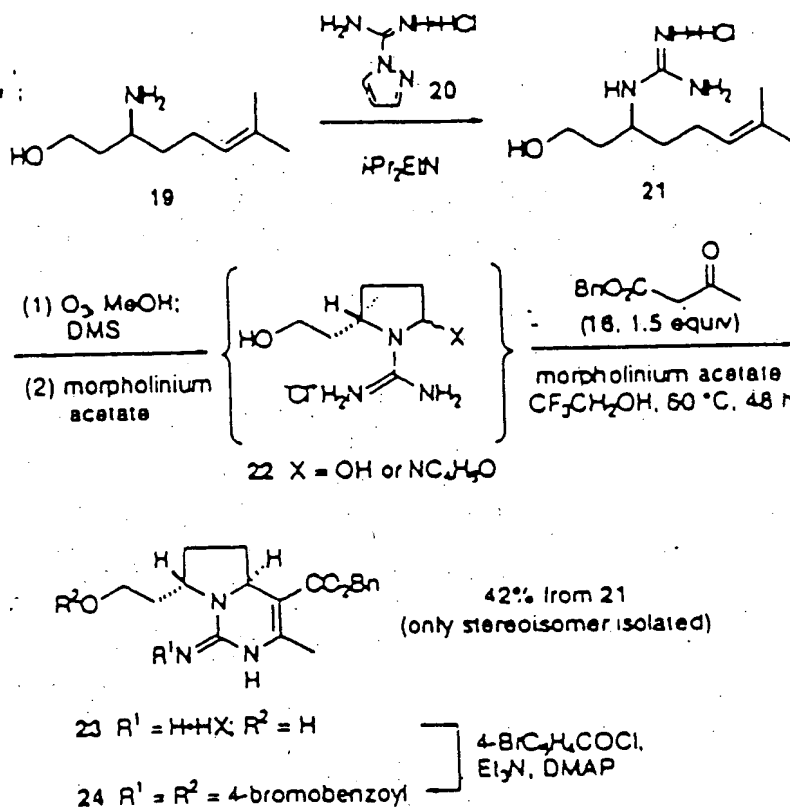
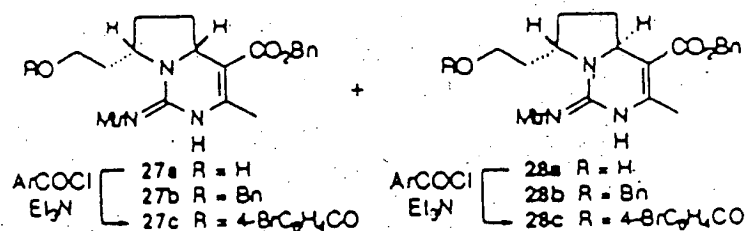
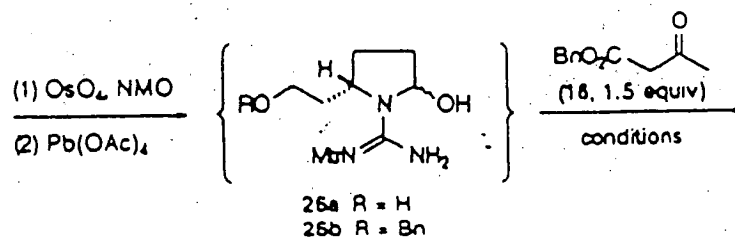
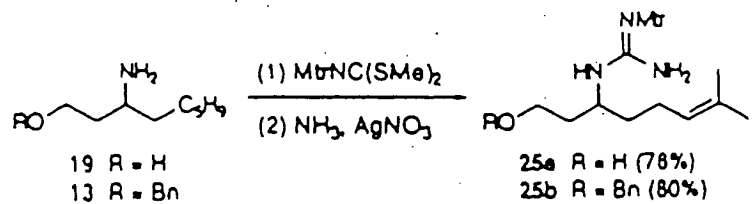


FIGURE 5



| substrate | reaction conditions | 27:28 (yield) ^a |
|-----------|----------------------------------------------------|----------------------------|
| 25a | morpholinium acetate (1.5 eq), | 6:1 (61%) |
| 25b | CF ₃ CH ₂ OH, 60 °C, 48 h | 7:1 (84%) |
| 25b | PPE, CH ₂ Cl ₂ , 23 °C, 48 h | 1:20 (61%) |

^a Combined overall yield of 27 and 28 from 25.

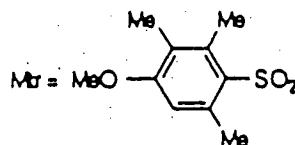


FIGURE 6

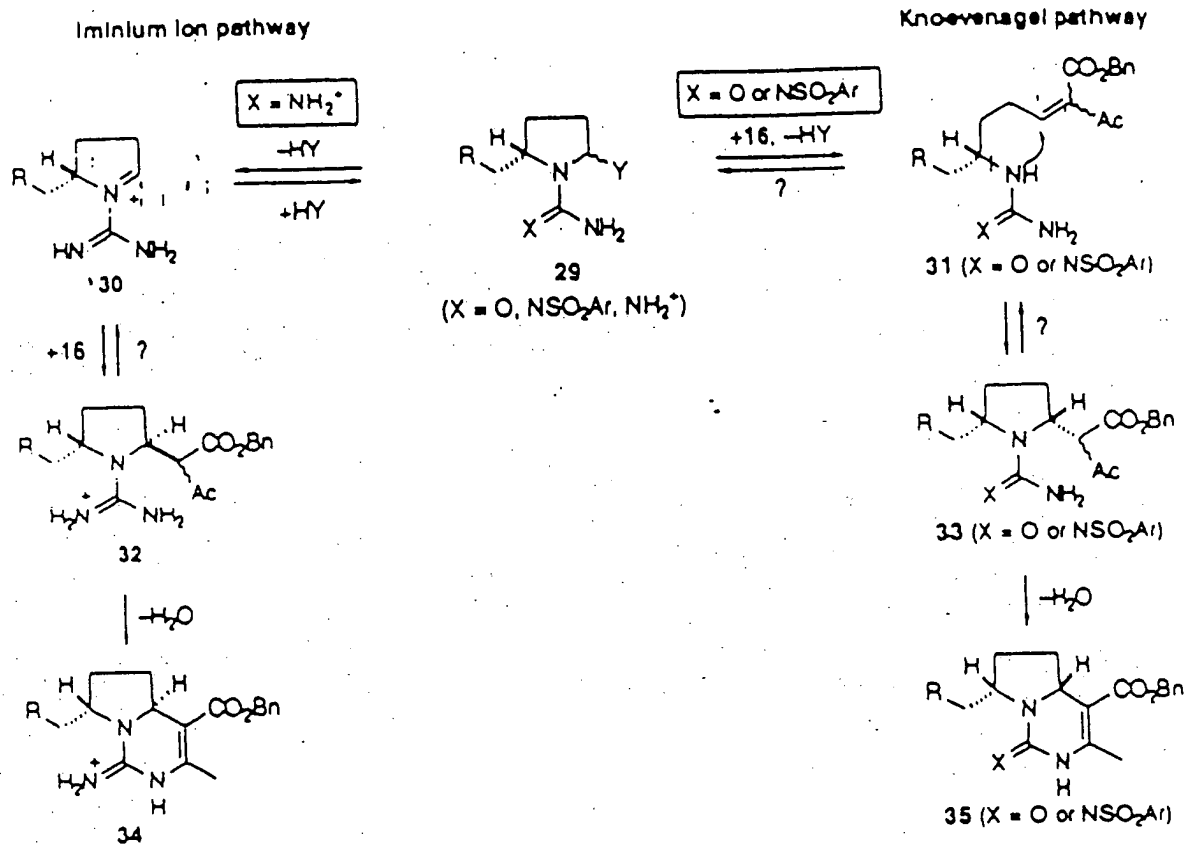


FIGURE 7

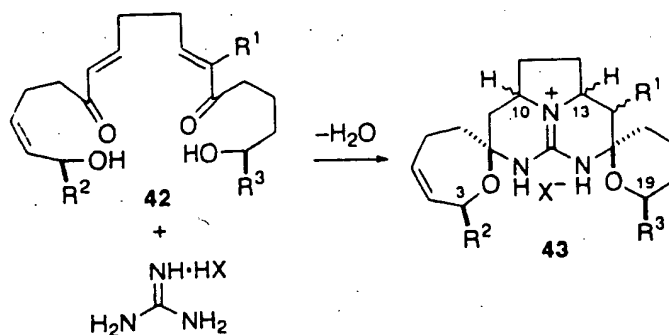
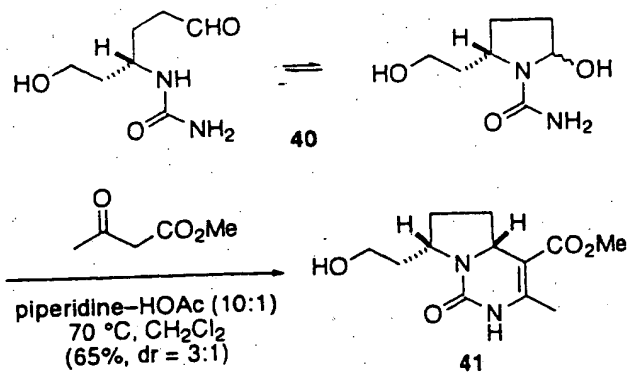
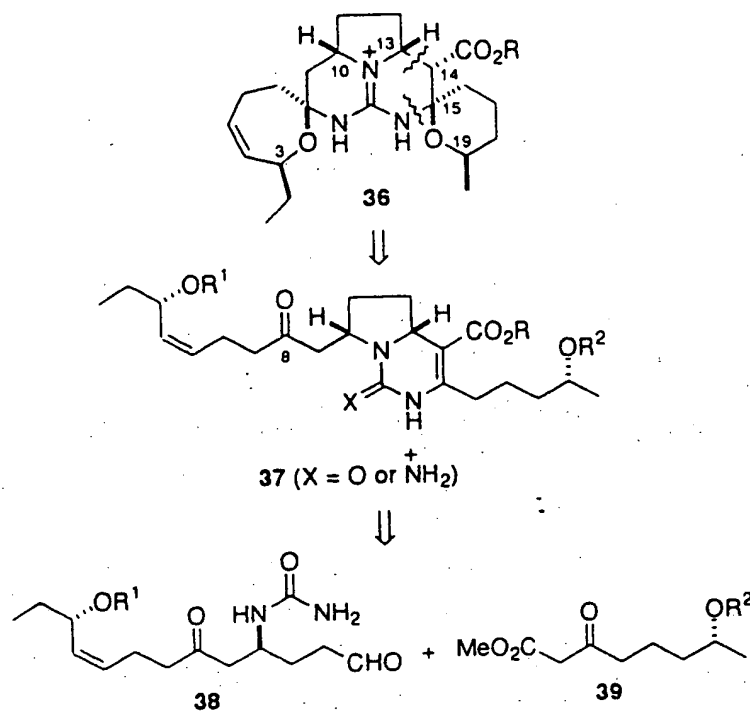


Figure 8

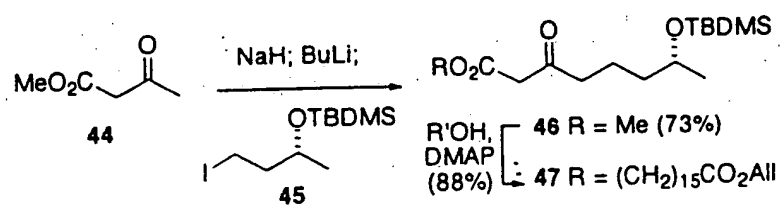


Figure 9

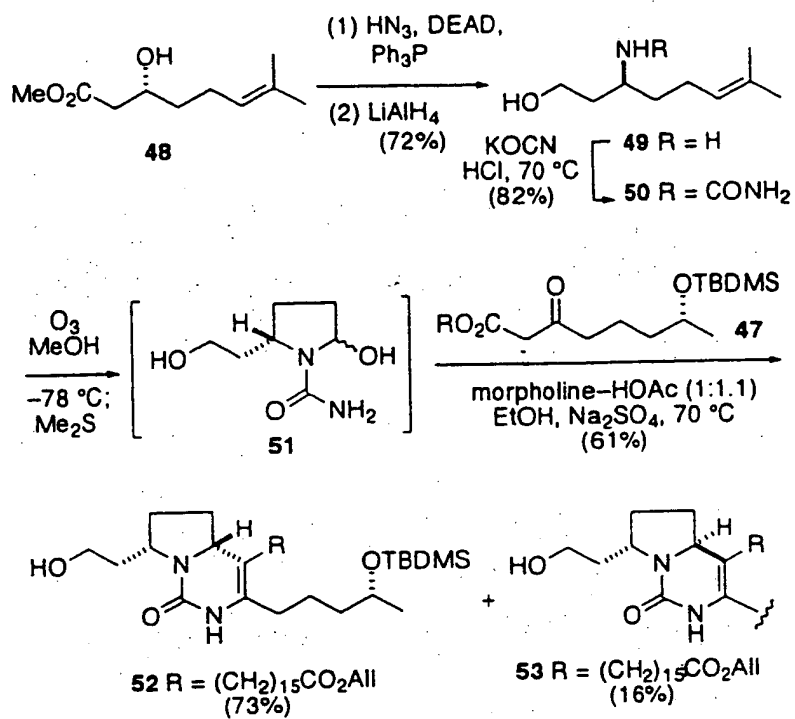


Figure 10

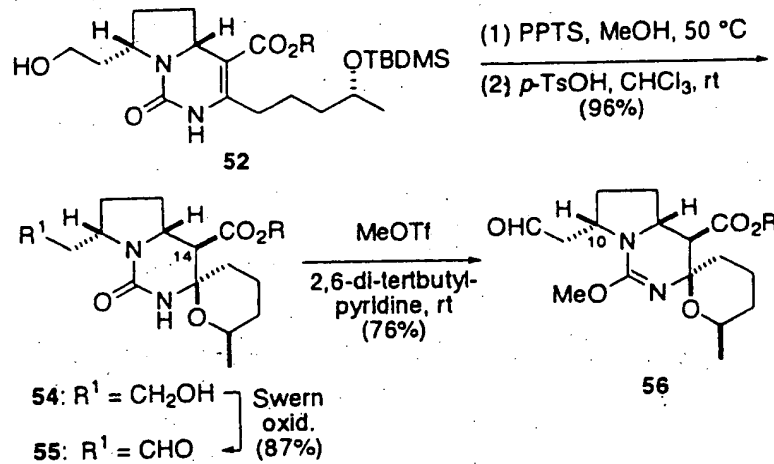


Figure 11

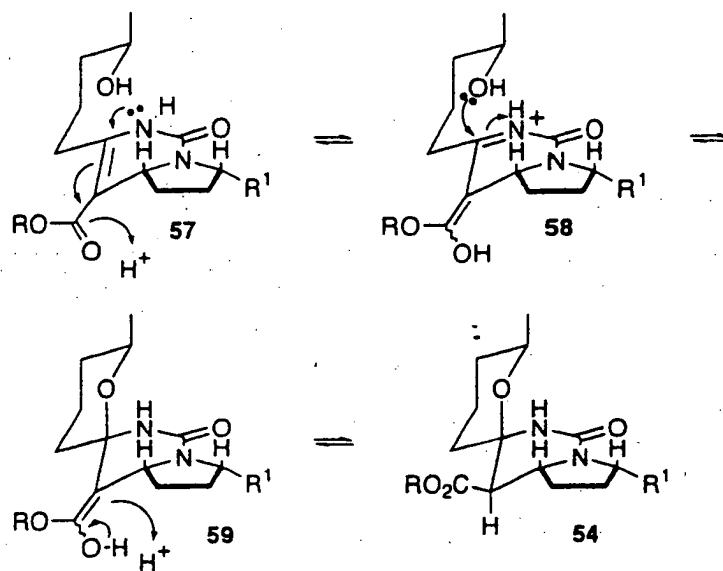


Figure 12

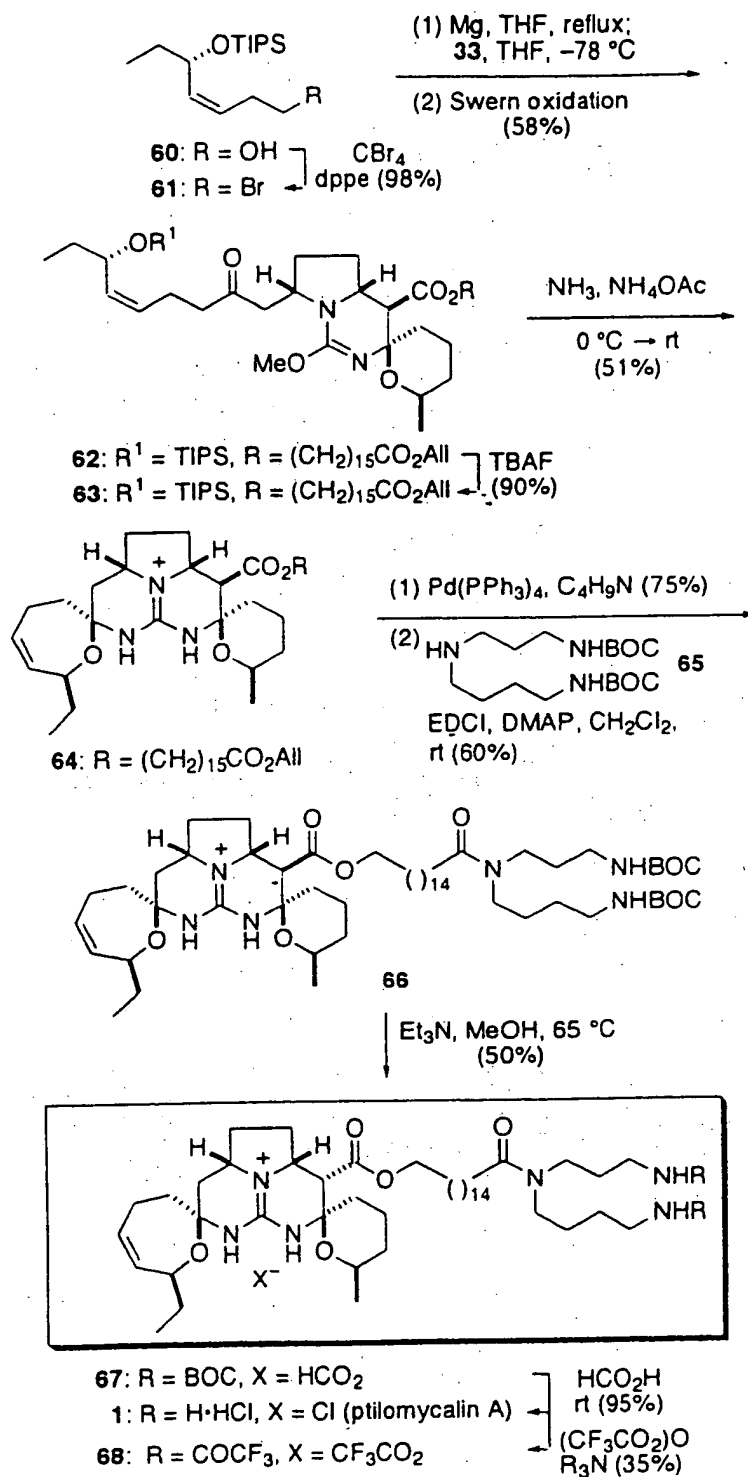


Figure 13

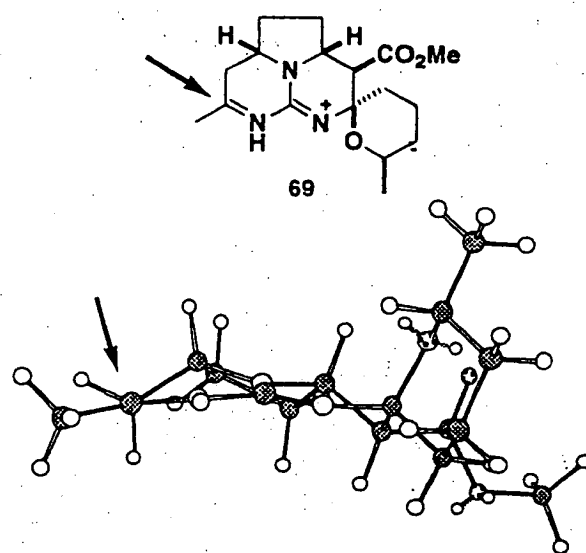


Figure 14

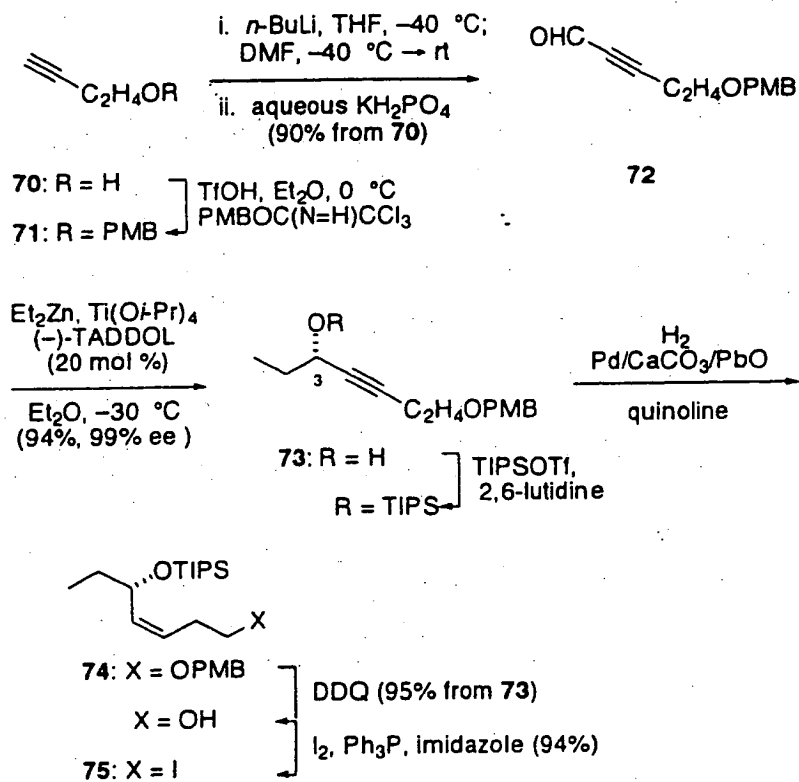


Figure 15

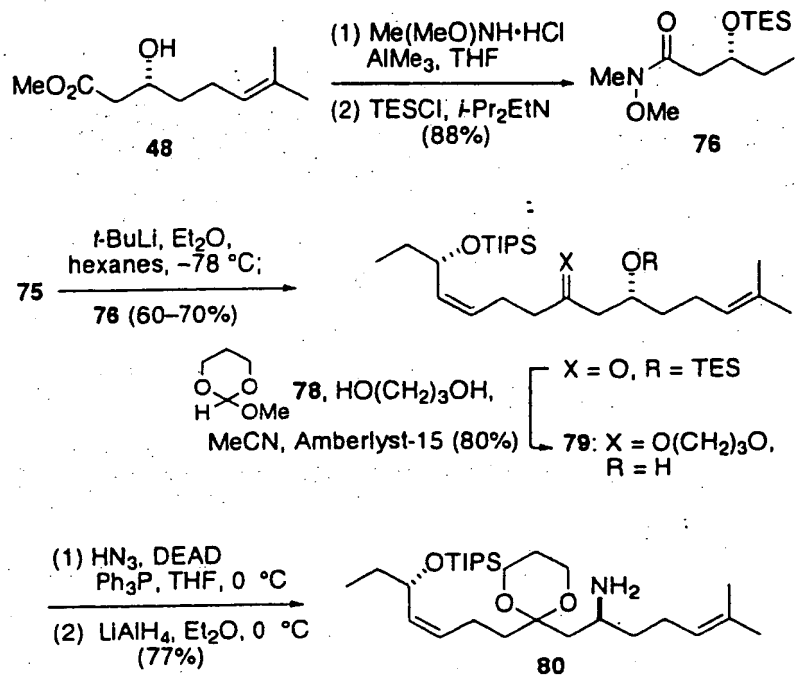


Figure 16

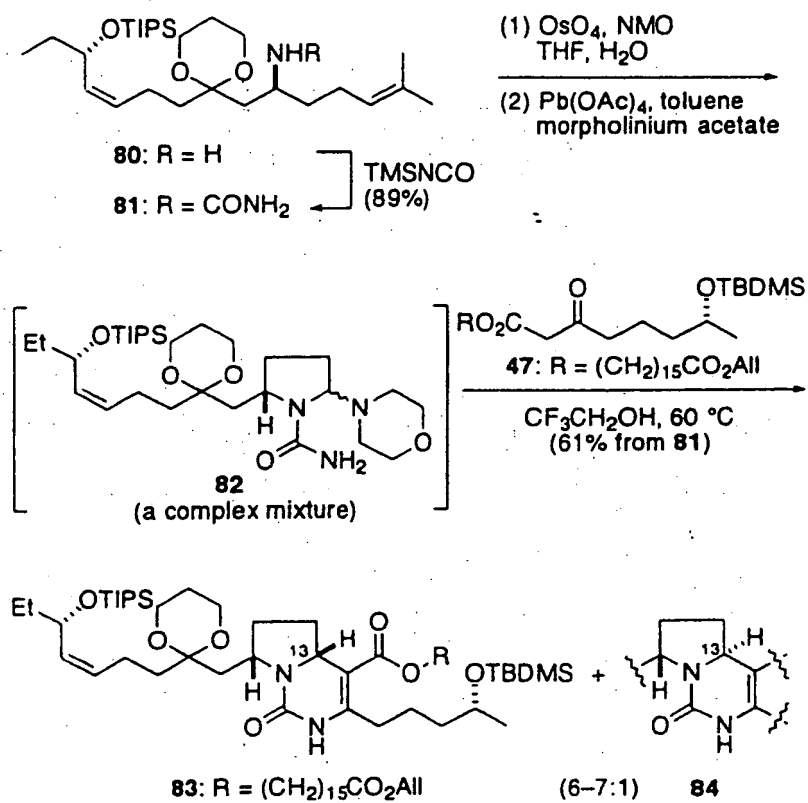


Figure 17

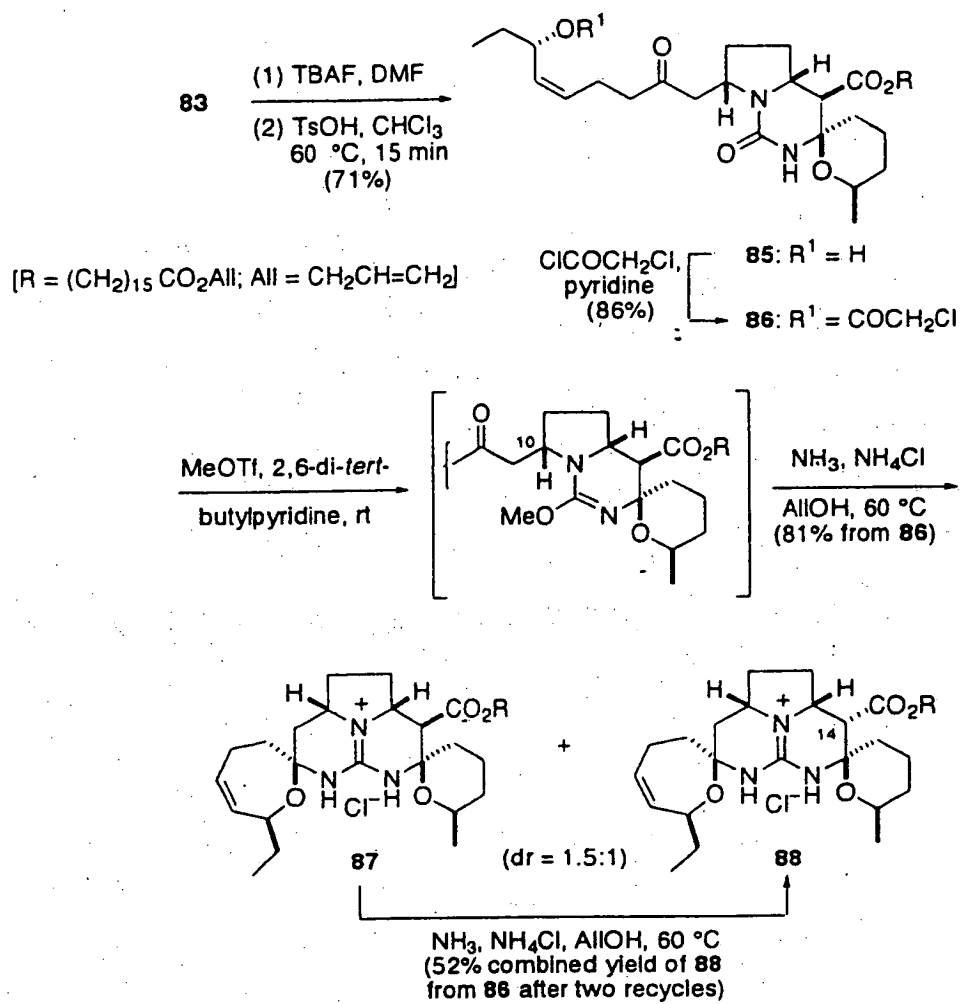


Figure 18

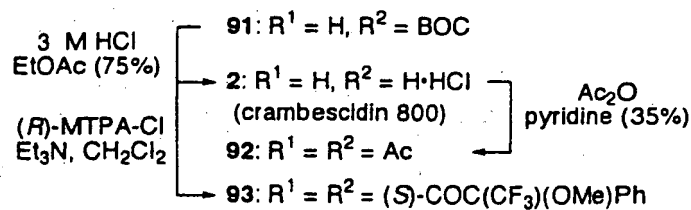
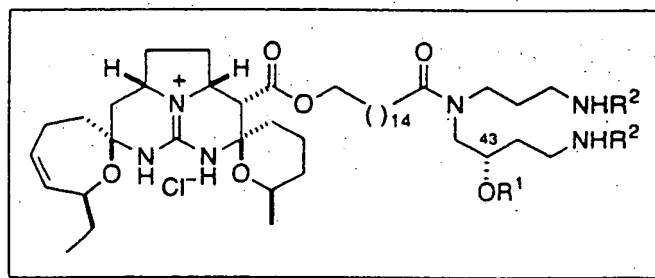
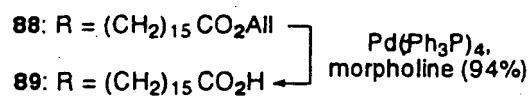
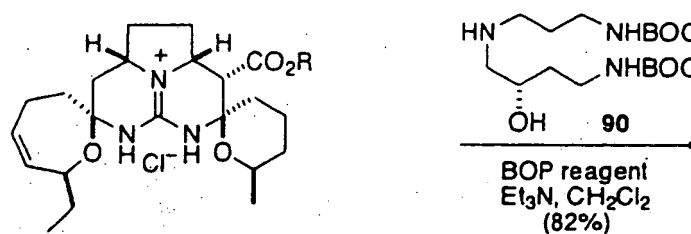
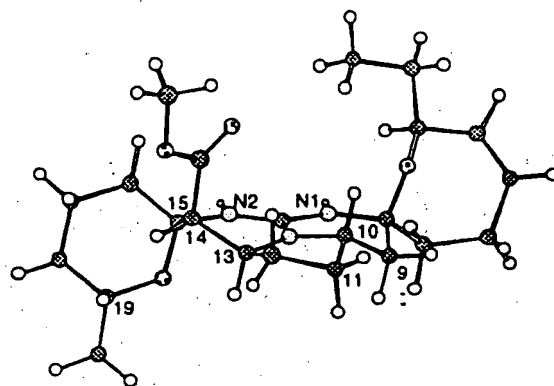
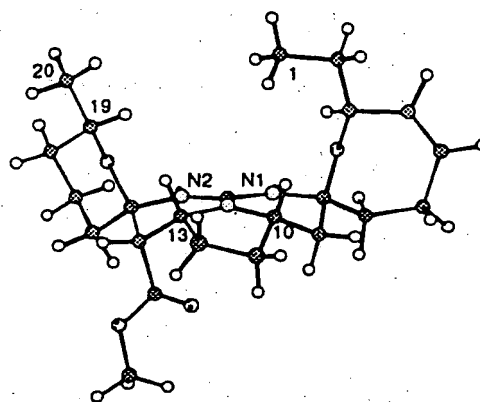


Figure 19



13,14,15-isocrambescidin core



crambescidin/ptilomycalin A core

Figure 20

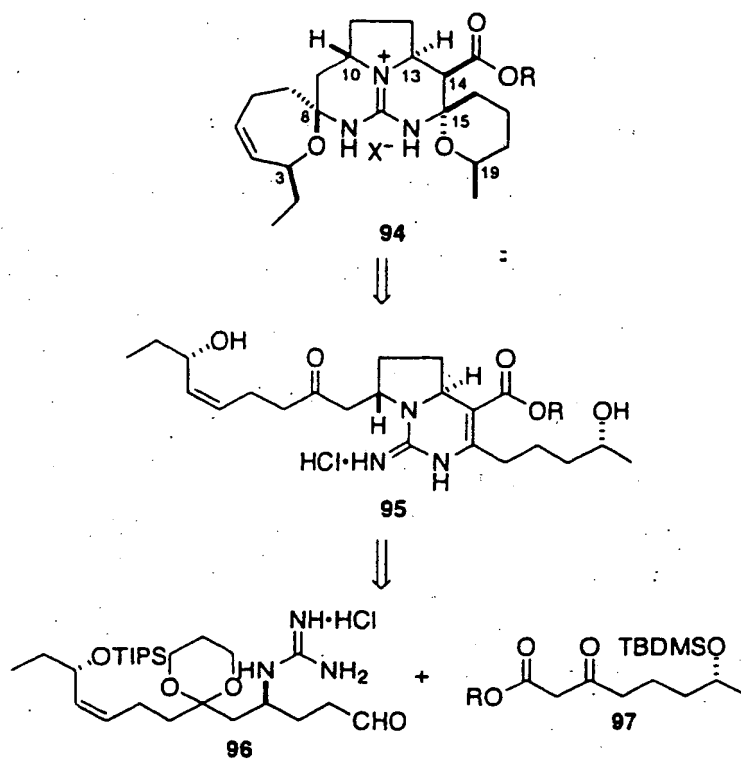


Figure 21

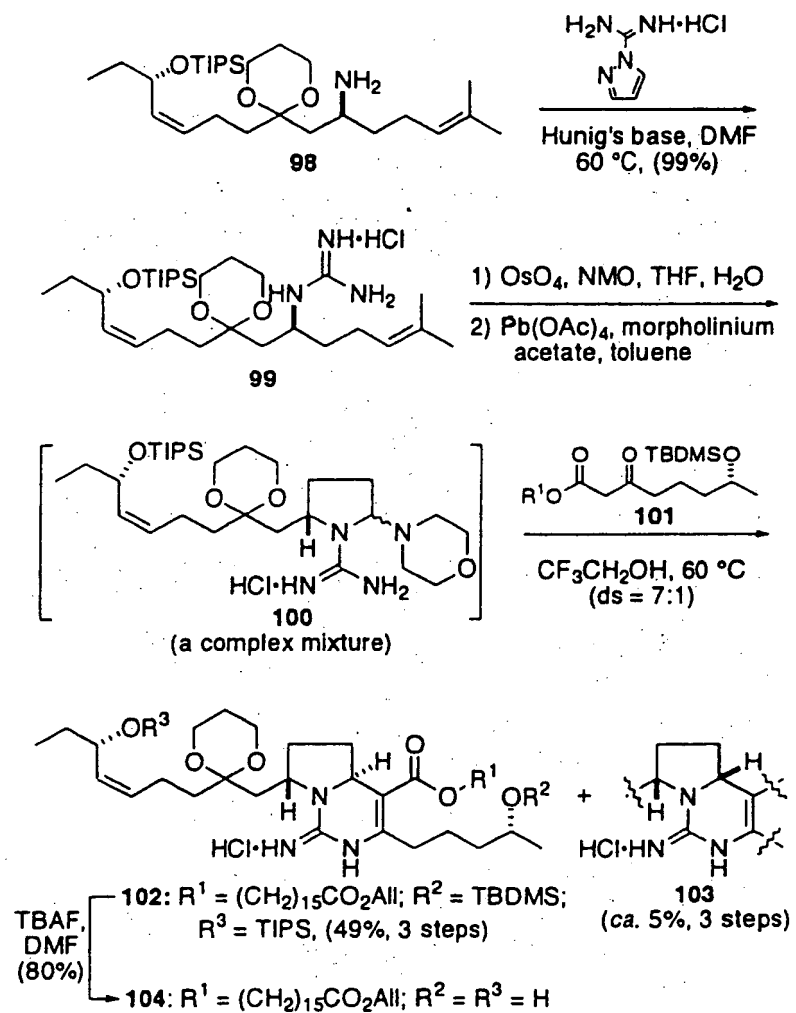


Figure 22

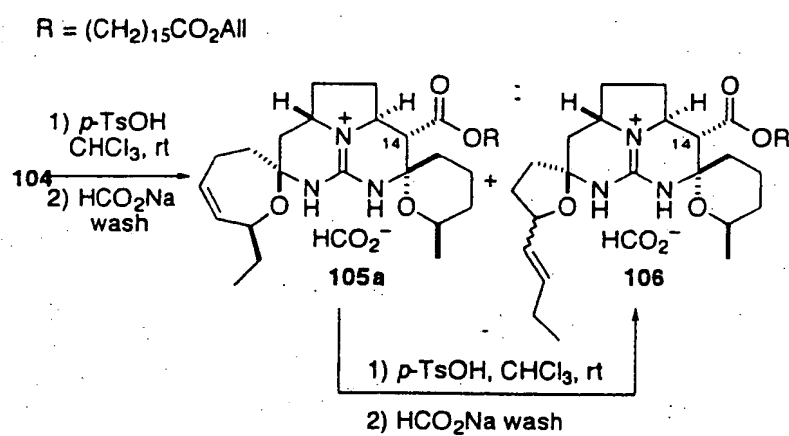


Figure 23

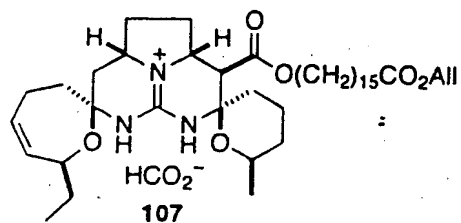
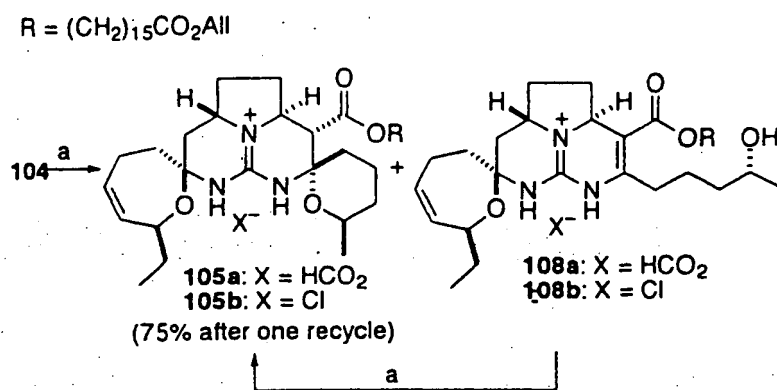


Figure 24



^aReagents: (a) PPTS, CHCl₃, 90 °C, 24 h; HCO₂ Na wash
or 0.1 N HCl wash

Figure 25

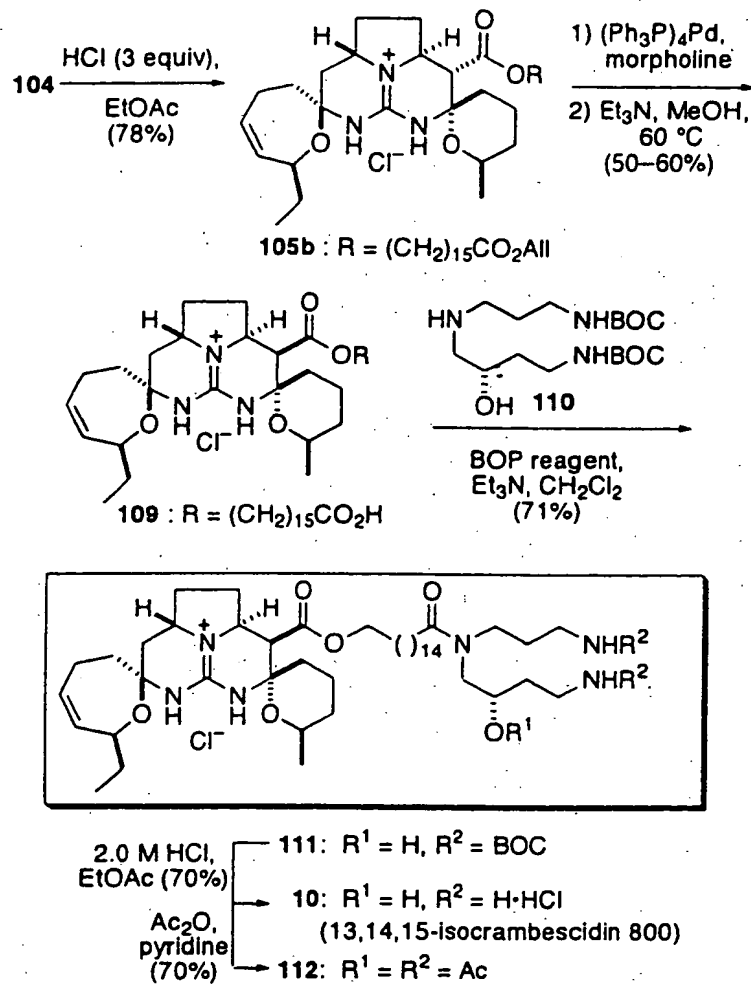


Figure 26



Figure 27

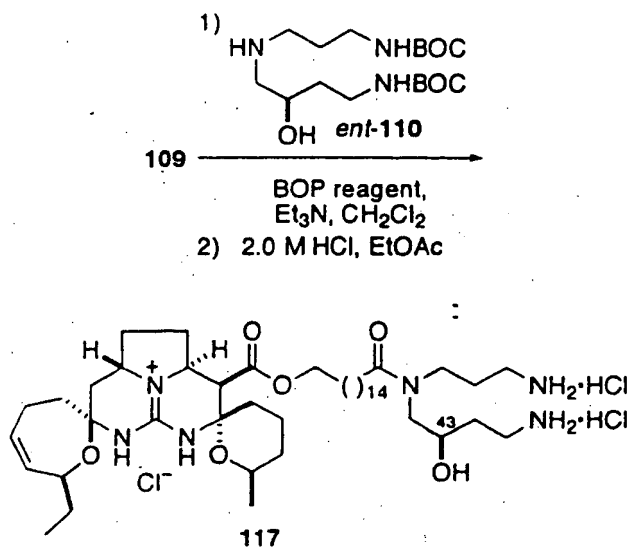


Figure 28

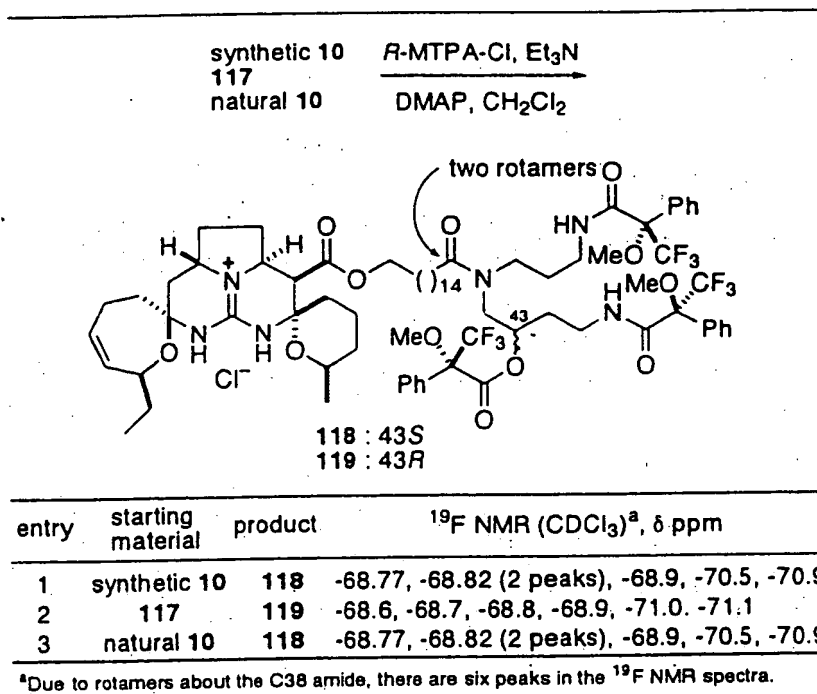


Figure 29

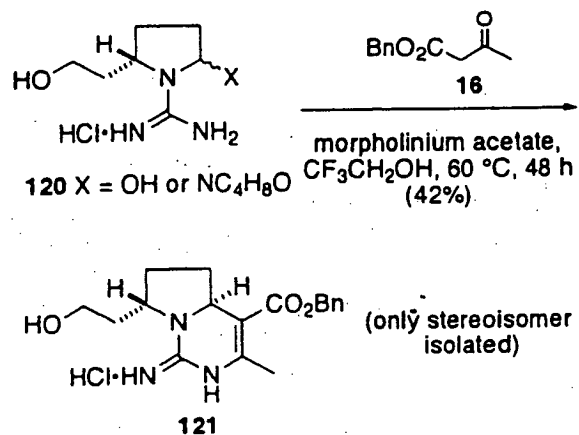
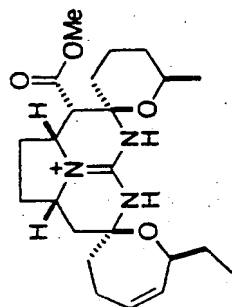
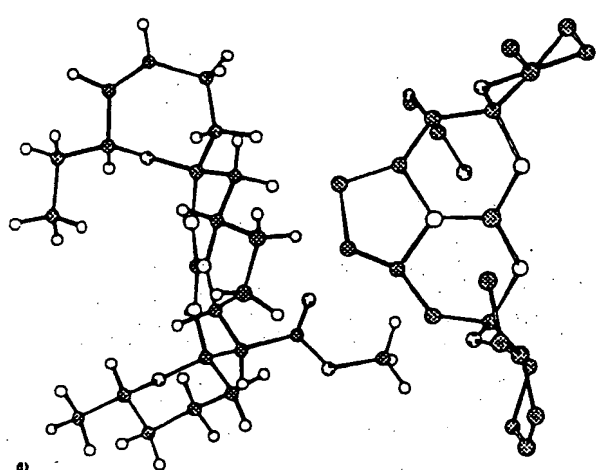


Figure 30

13,14,15-Isocrambescidin core



13,15-epicrambescadin core

13-epicrambescidin core

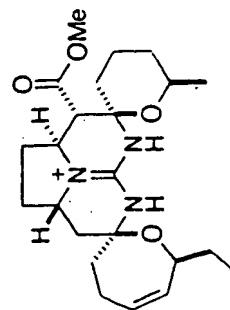
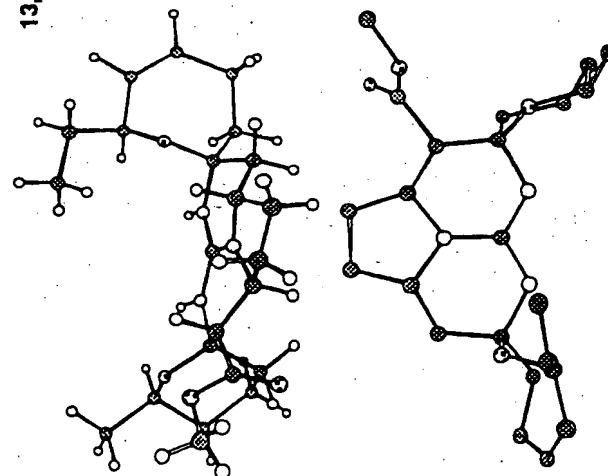
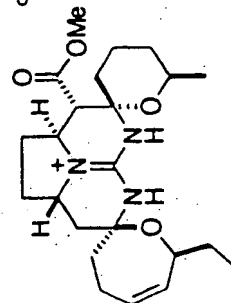
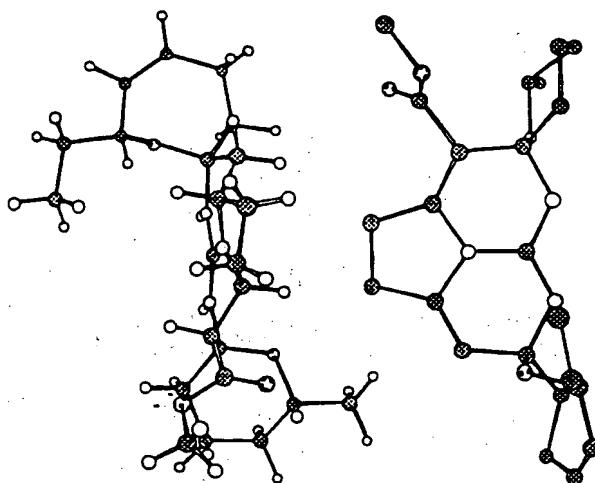


Figure 31

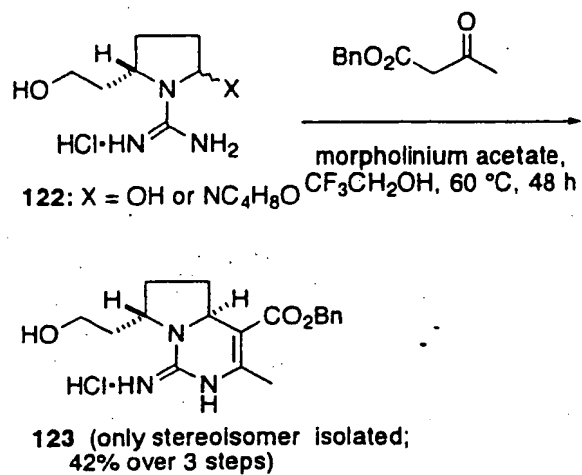


Figure 32

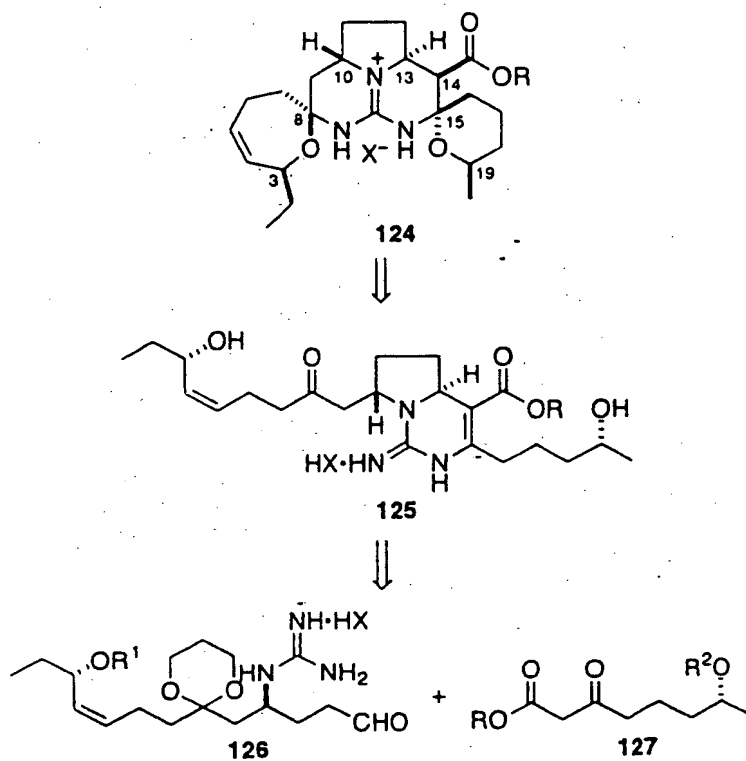


Figure 33

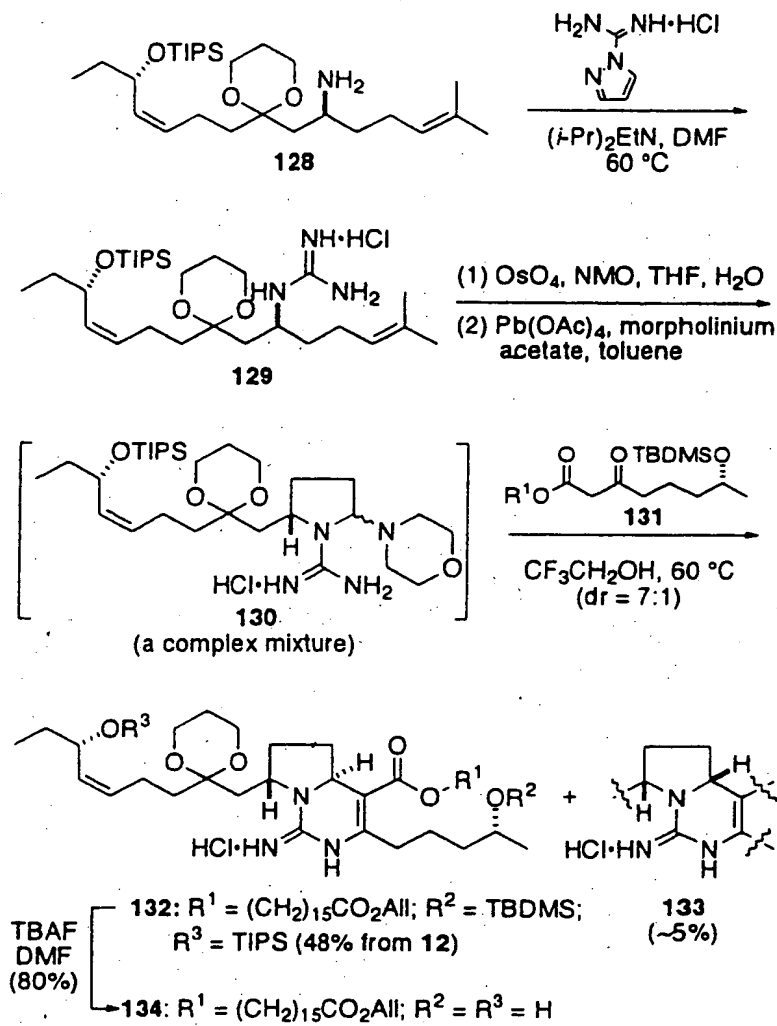


Figure 34

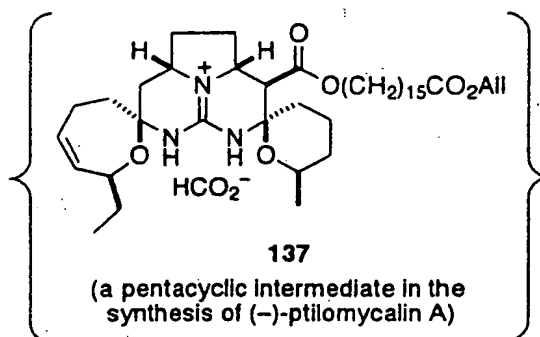
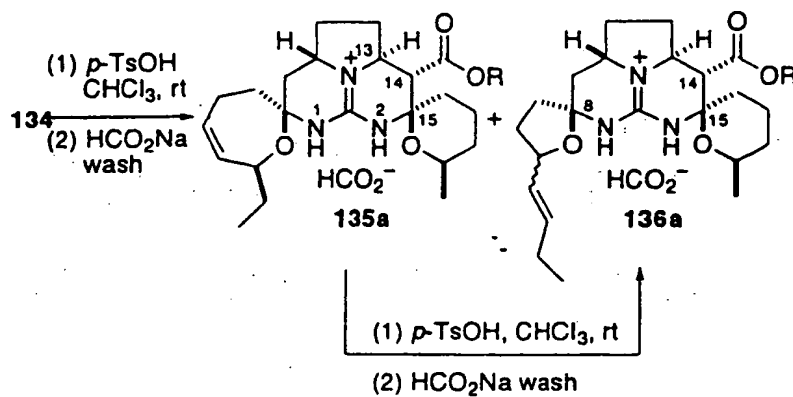
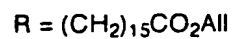
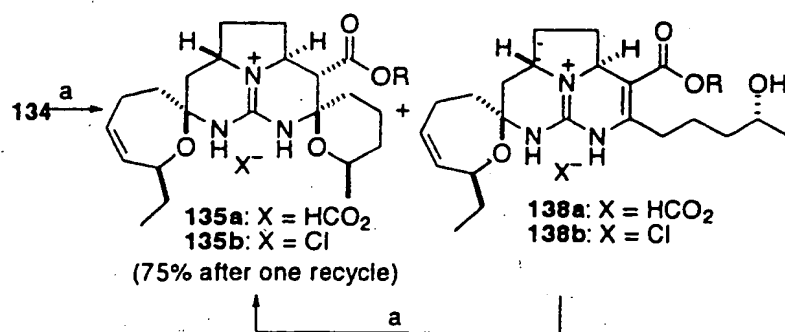


Figure 35

R = (CH₂)₁₅CO₂AlI



^aReagents: (a) PPTS, CHCl₃, 90 °C, 24 h; HCO₂Na wash
or 0.1 N HCl wash

Figure 36

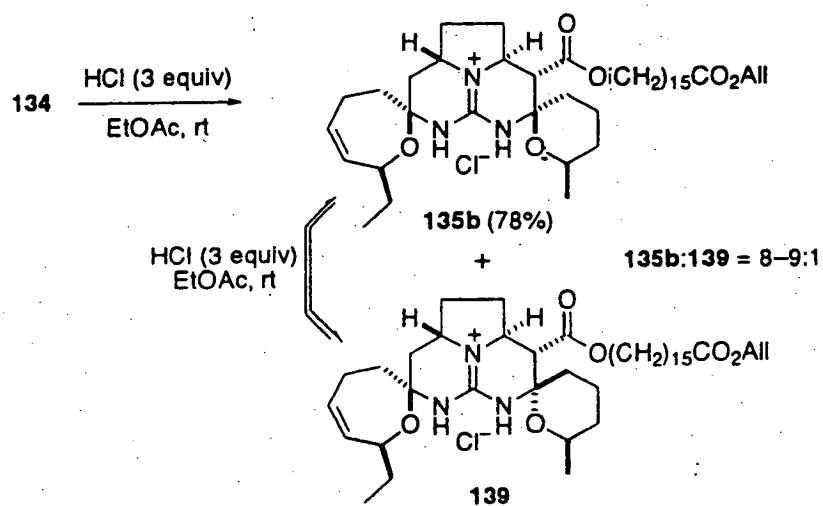


Figure 37

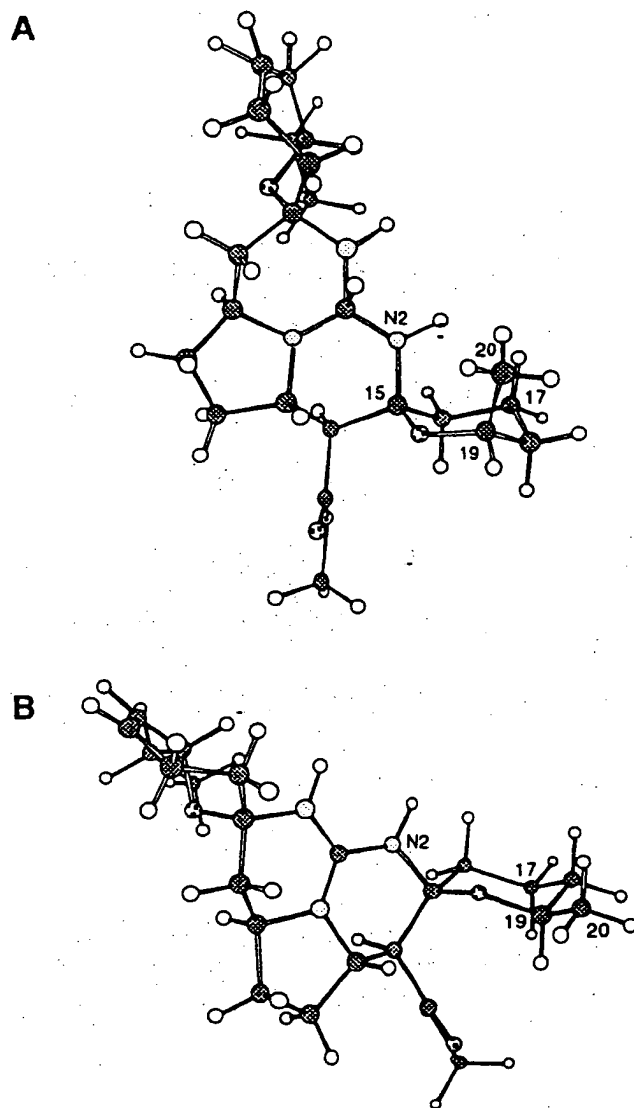


Figure 38

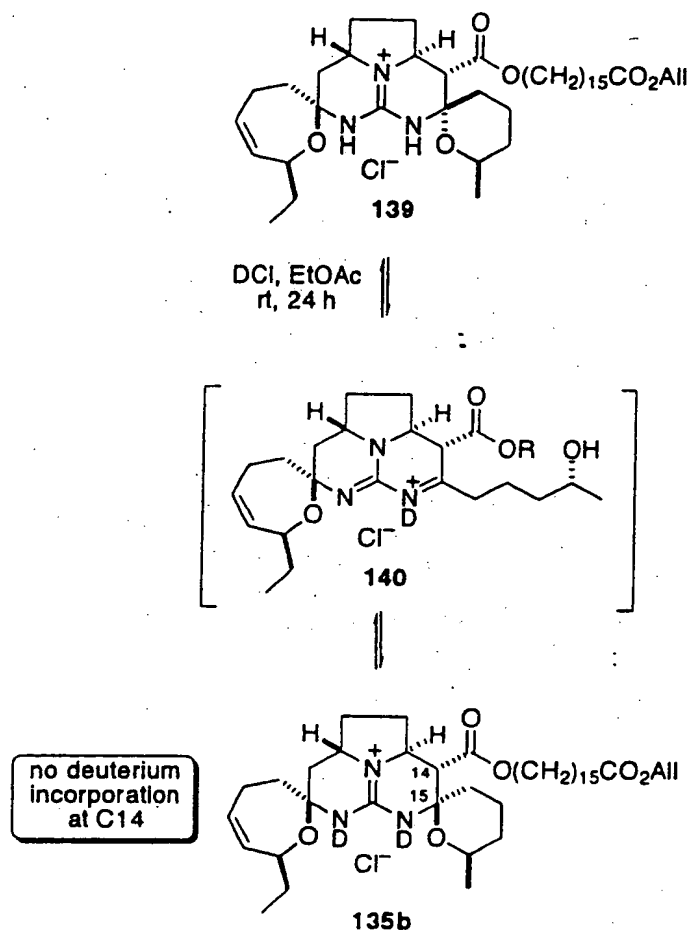


Figure 39

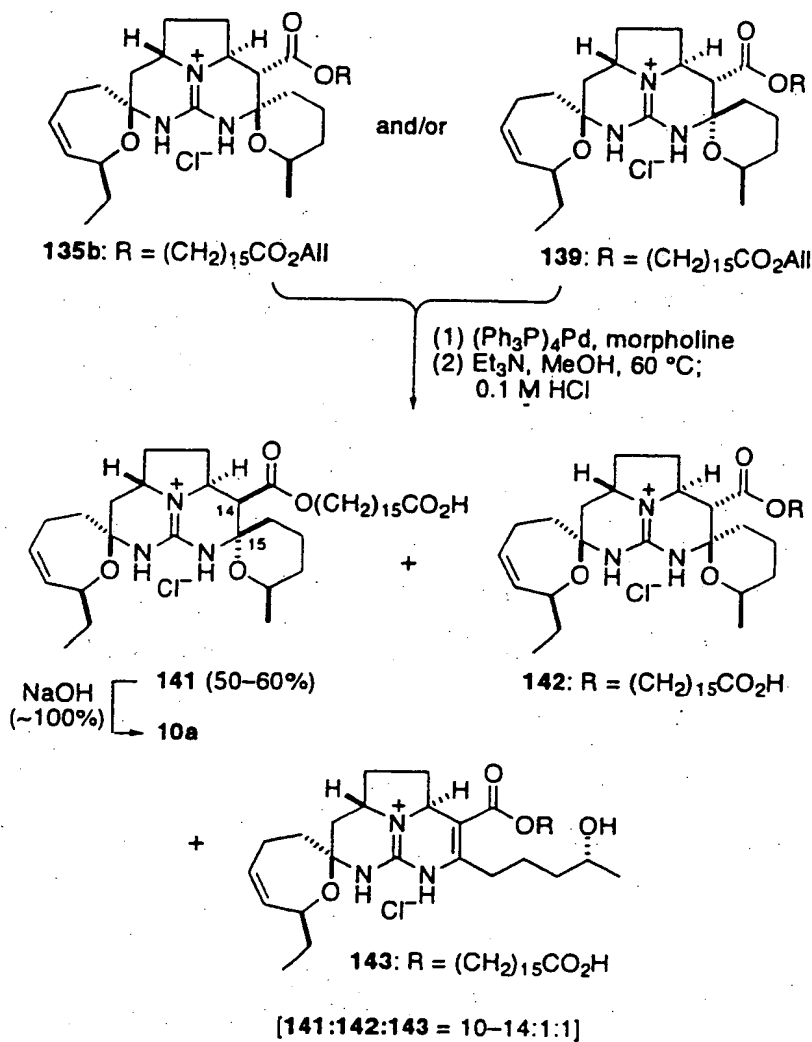


Figure 40

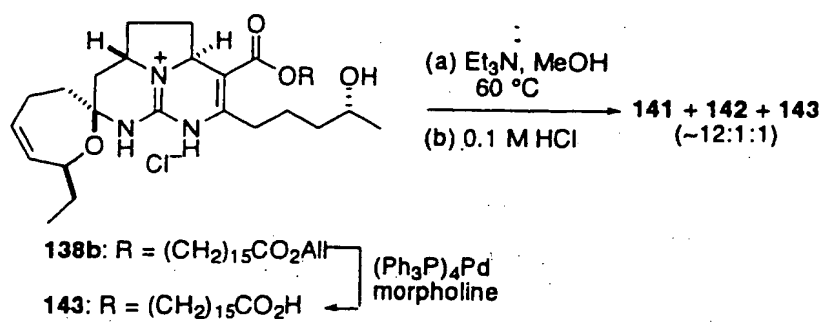


Figure 41

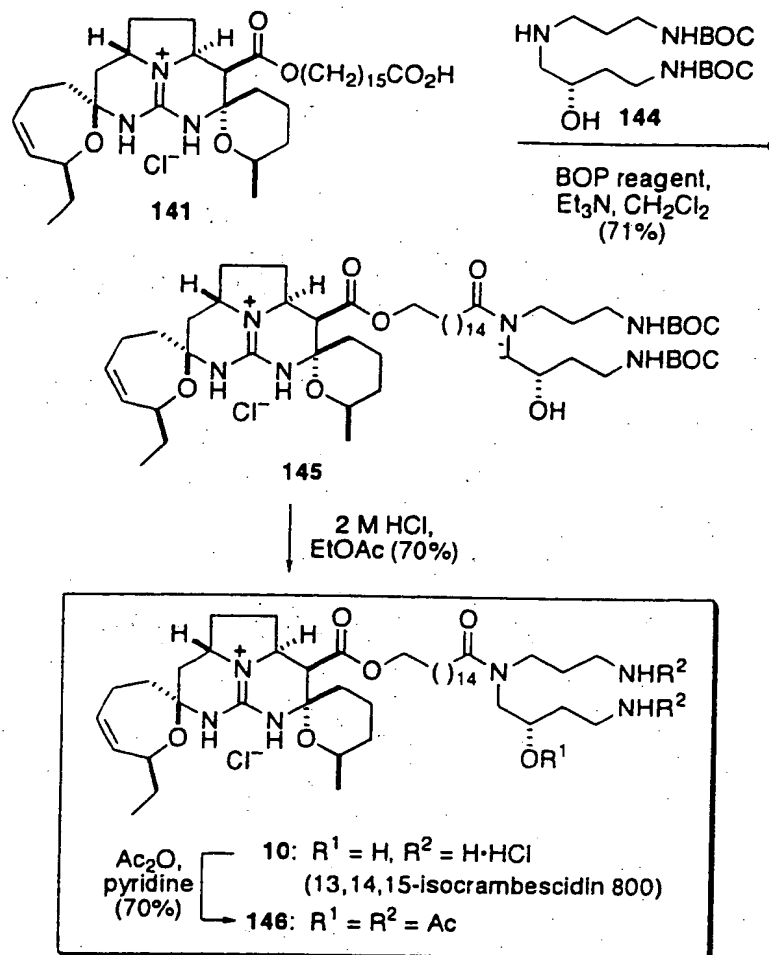


Figure 42

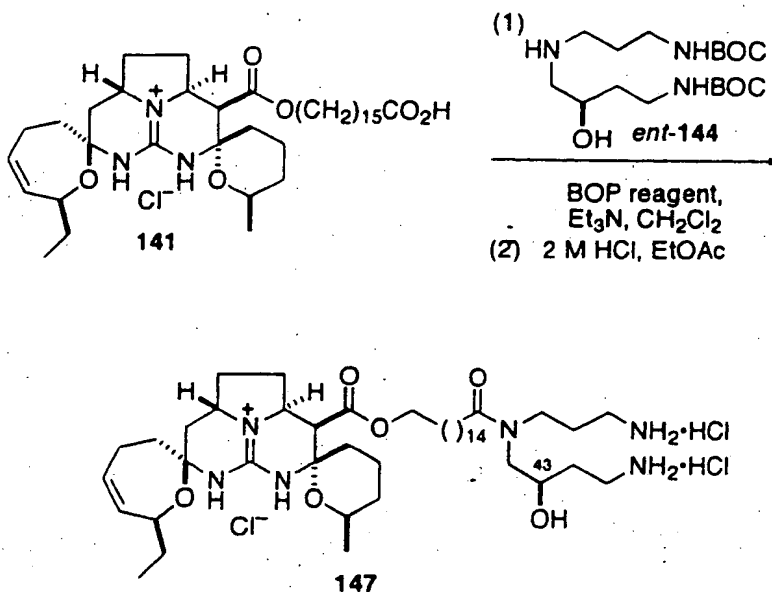
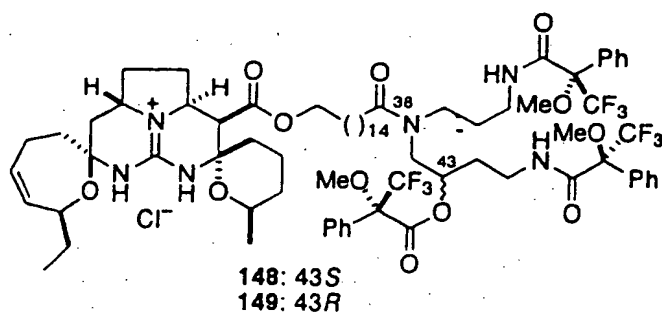


Figure 43



| entry | starting material | product | ^{19}F NMR (CDCl_3) ^a , δ ppm |
|-------|-------------------|---------|---------------------------------------------------------------------|
| 1 | synthetic 10 | 148 | -68.77, -68.82 (2 peaks), -68.9, -70.5, -70.9 |
| 2 | 147 | 149 | -68.6, -68.7, -68.8, -68.9, -71.0, -71.1 |
| 3 | natural 10 | 148 | -68.77, -68.82 (2 peaks), -68.9, -70.5, -70.9 |

^aDue to rotamers about the C38 amide bond on the NMR time scale, six peaks are observed in the ^{19}F NMR spectra.

Figure 44

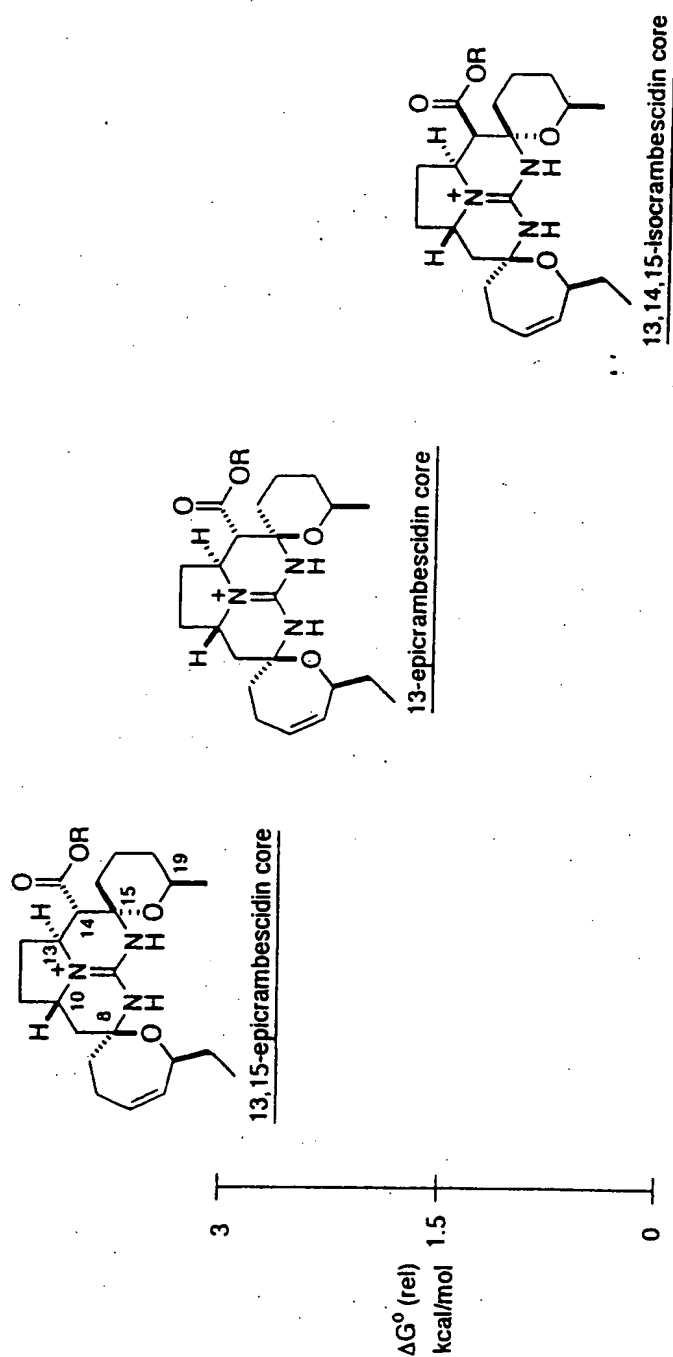


Figure 45

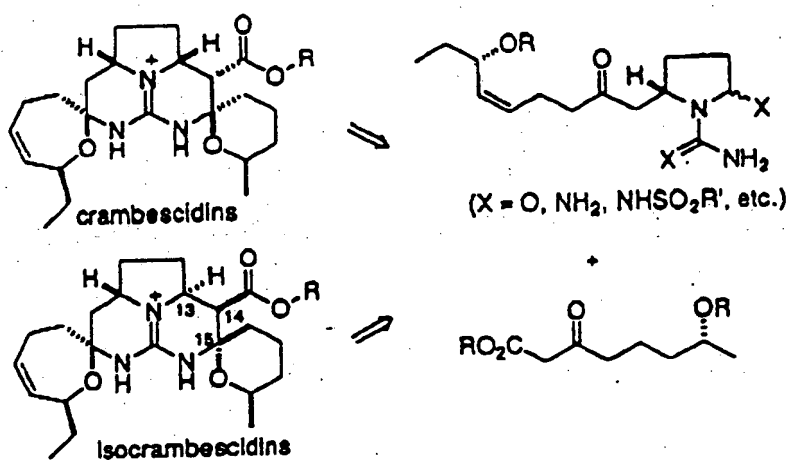


Figure 46

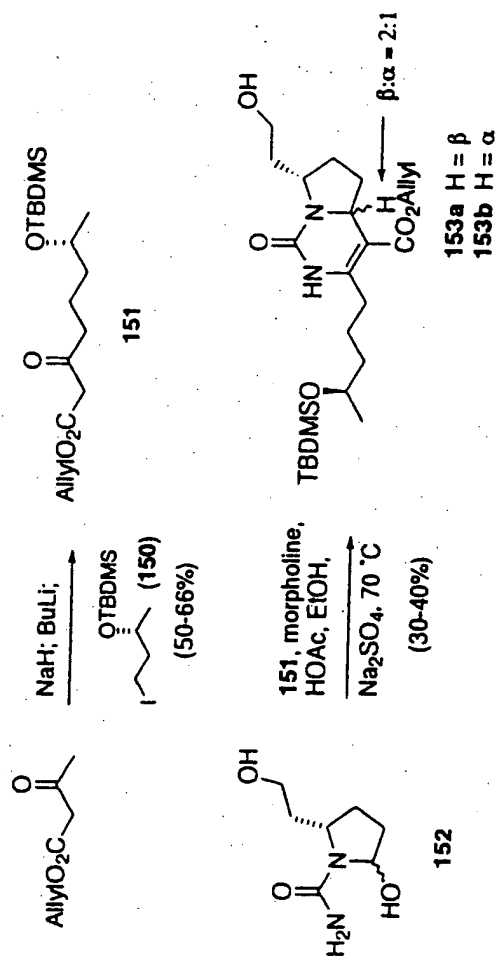


Figure 47

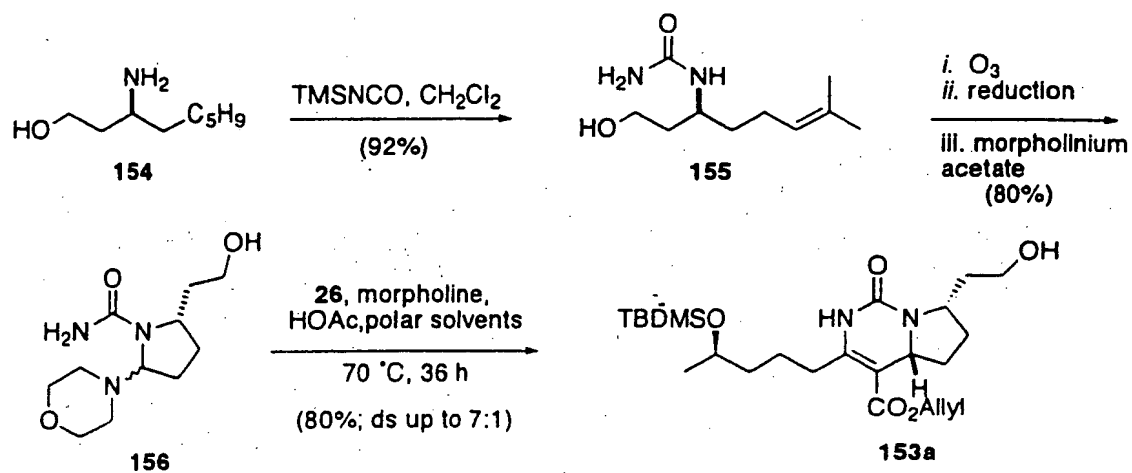


Figure 48

Figure 49

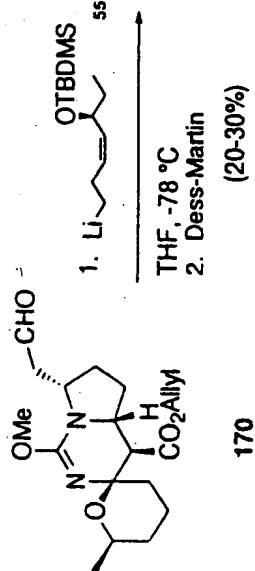


Figure 50.

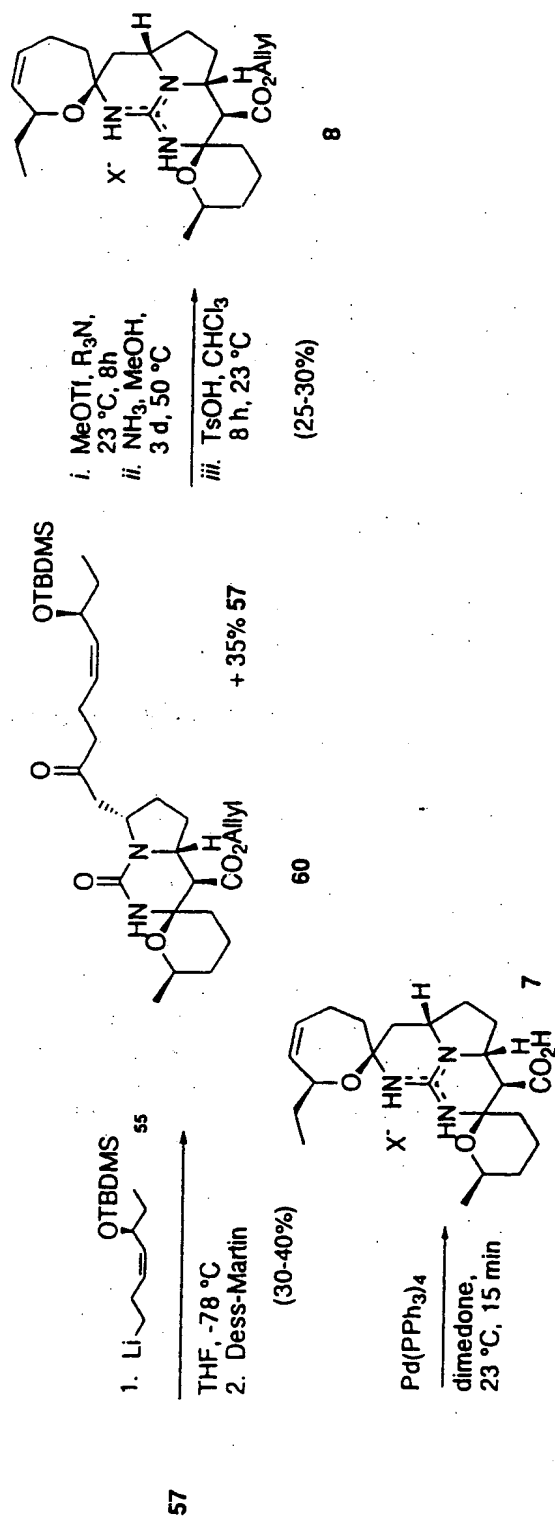


Figure 51

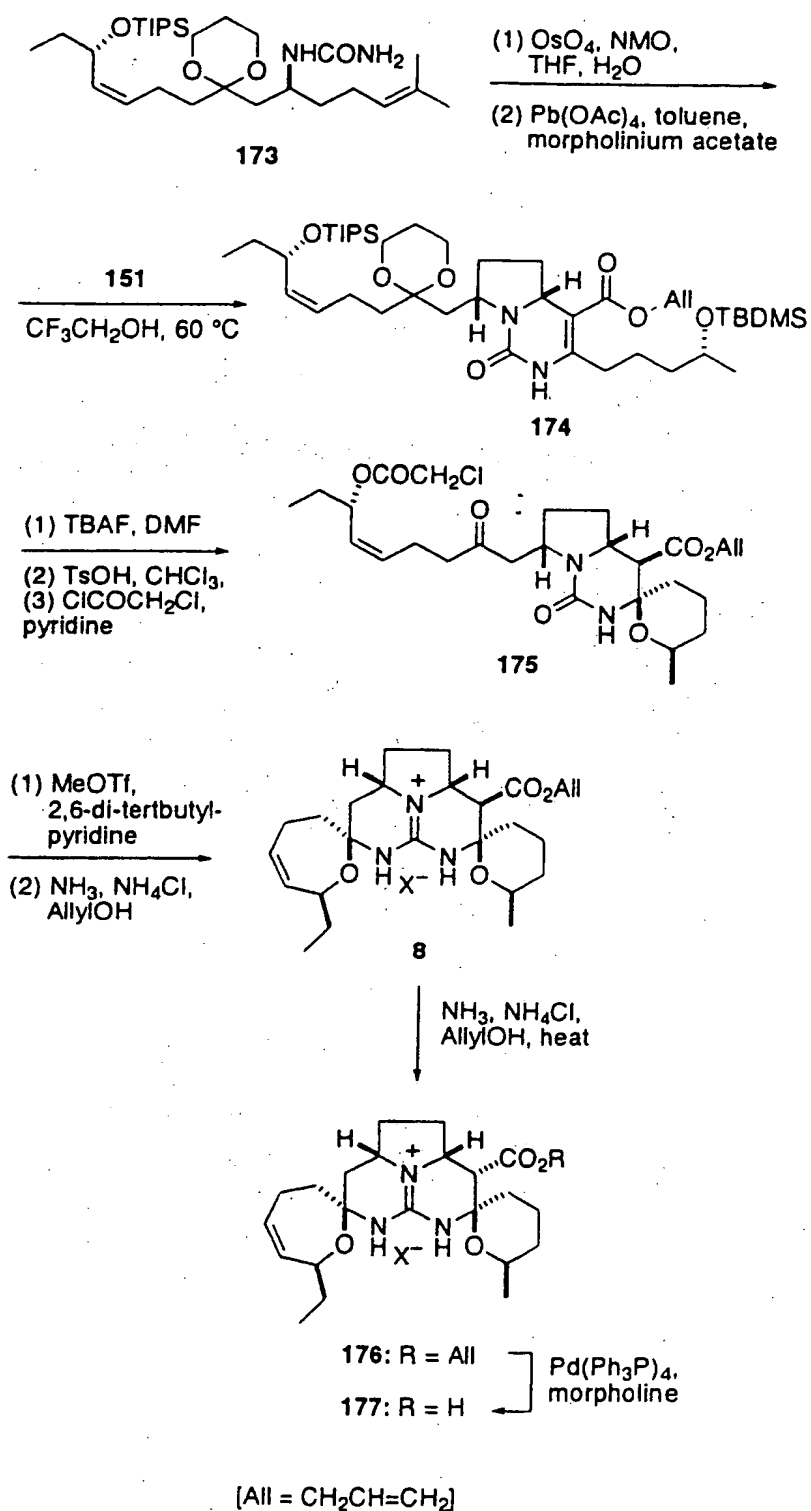


Figure 52

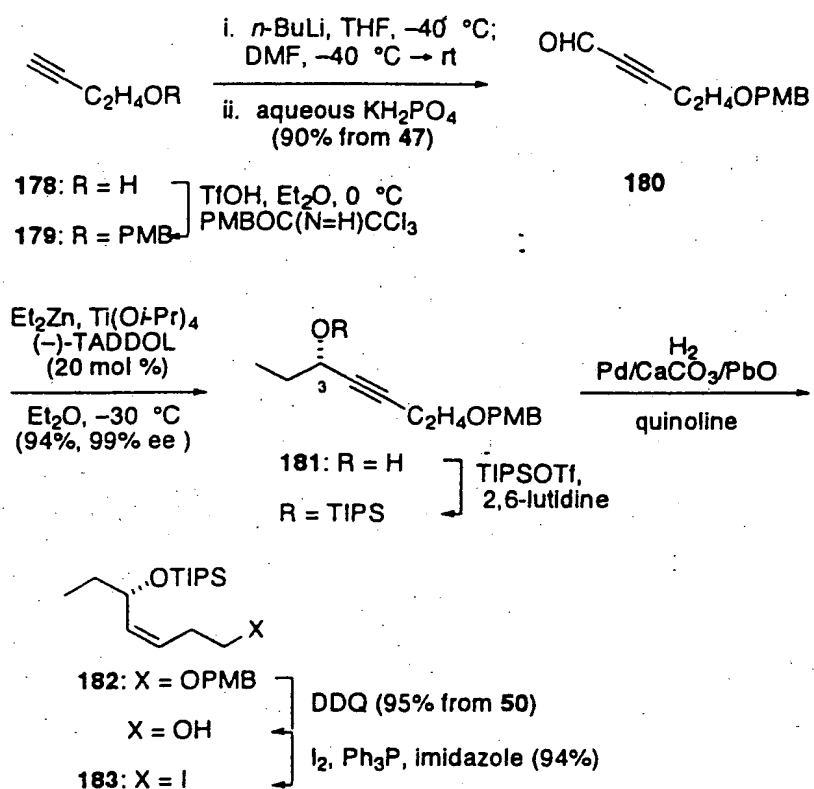


Figure 53

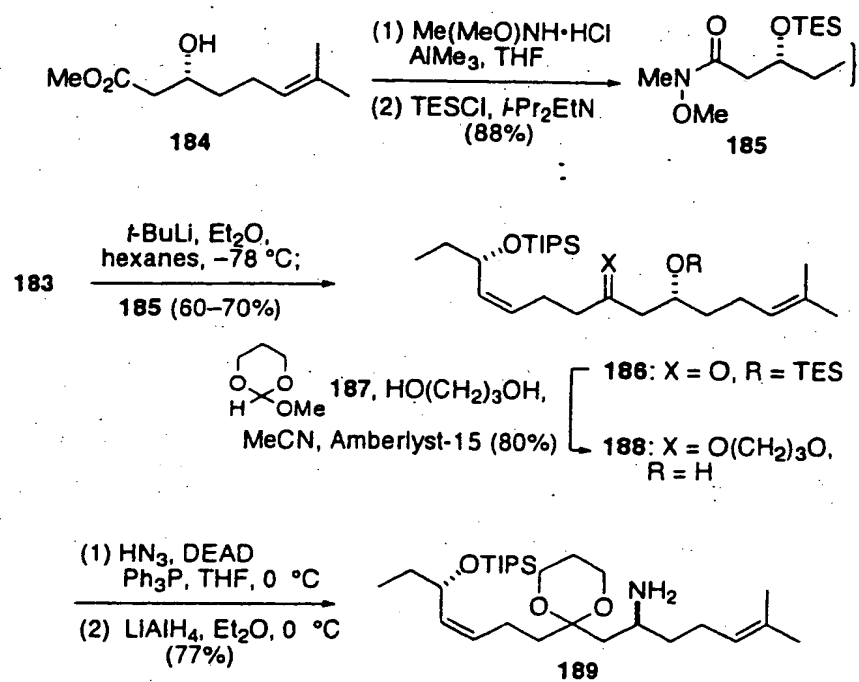


Figure 54

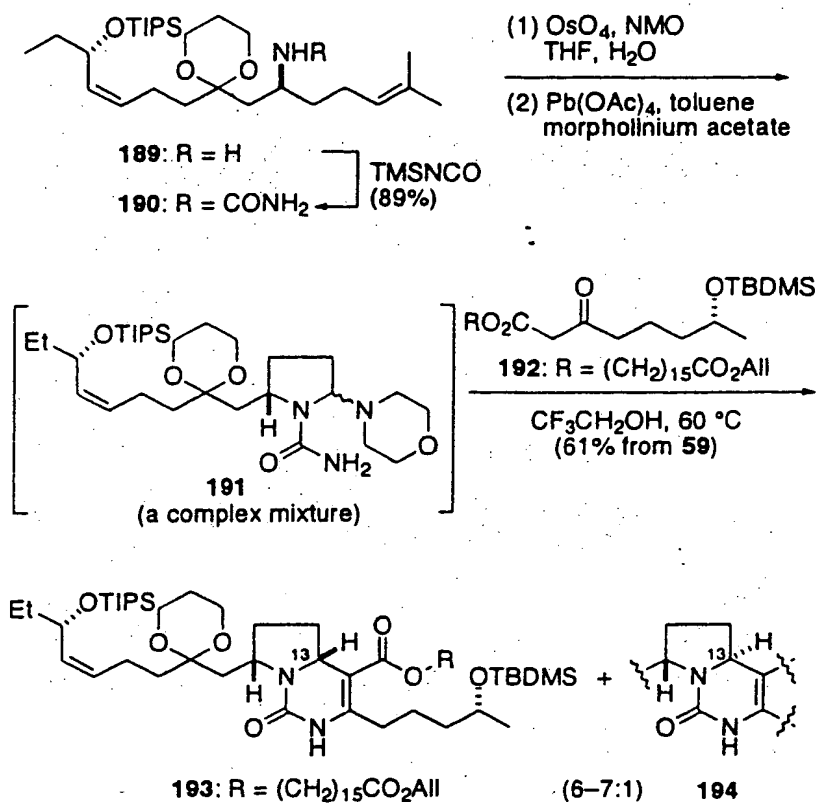


Figure 55

FIG. 56-A

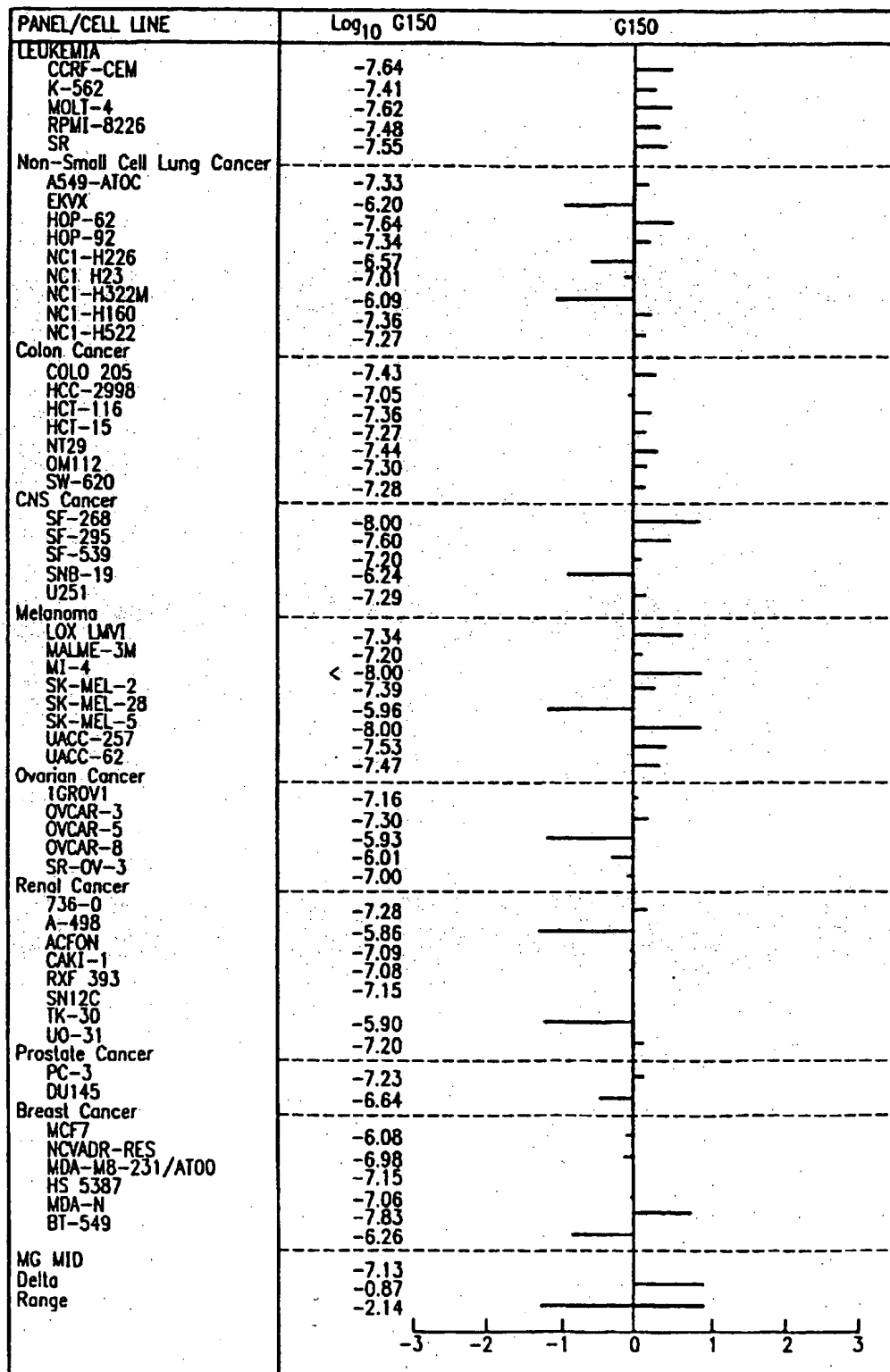


FIG. 56-B

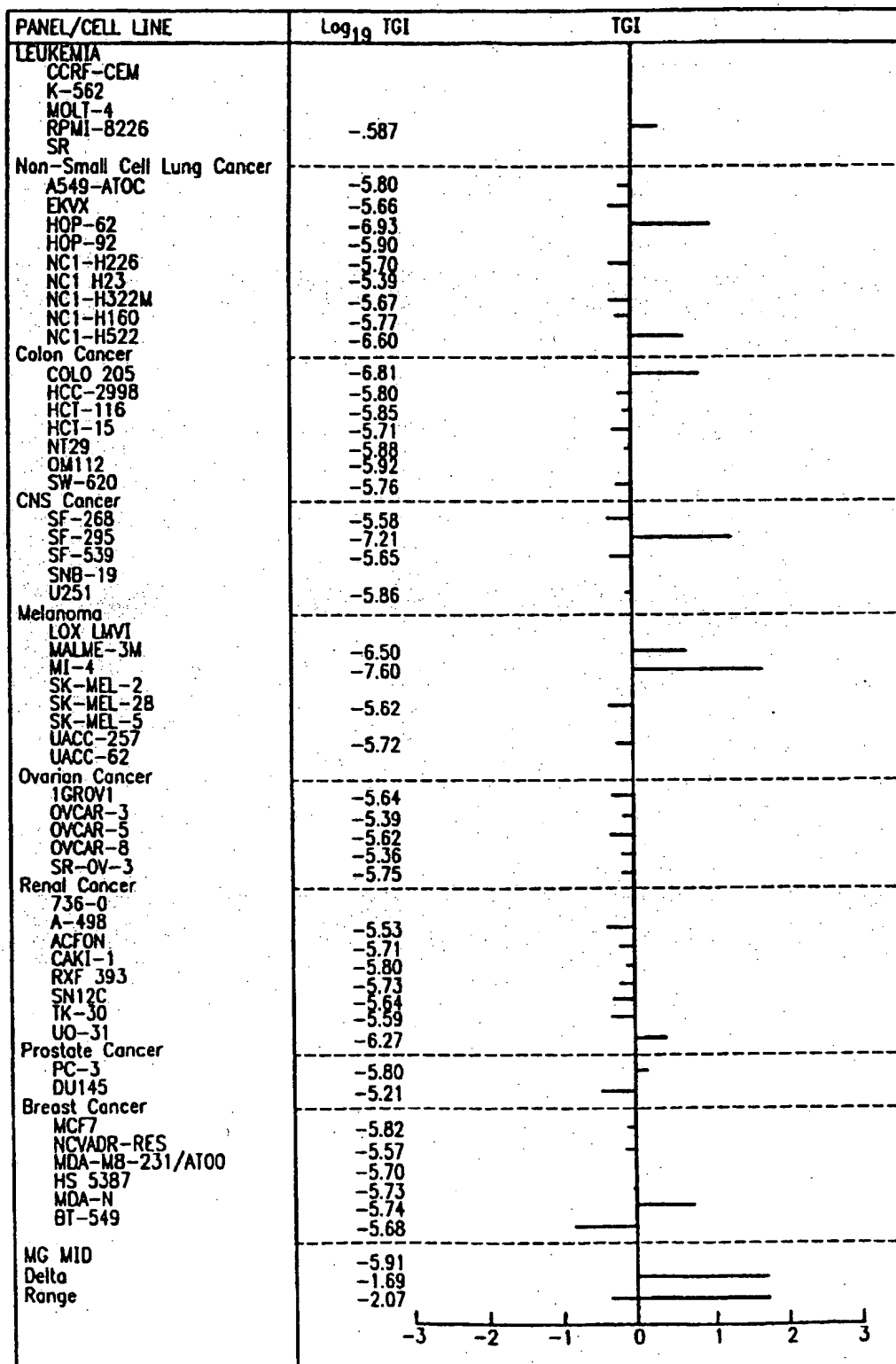


FIG. 56-C

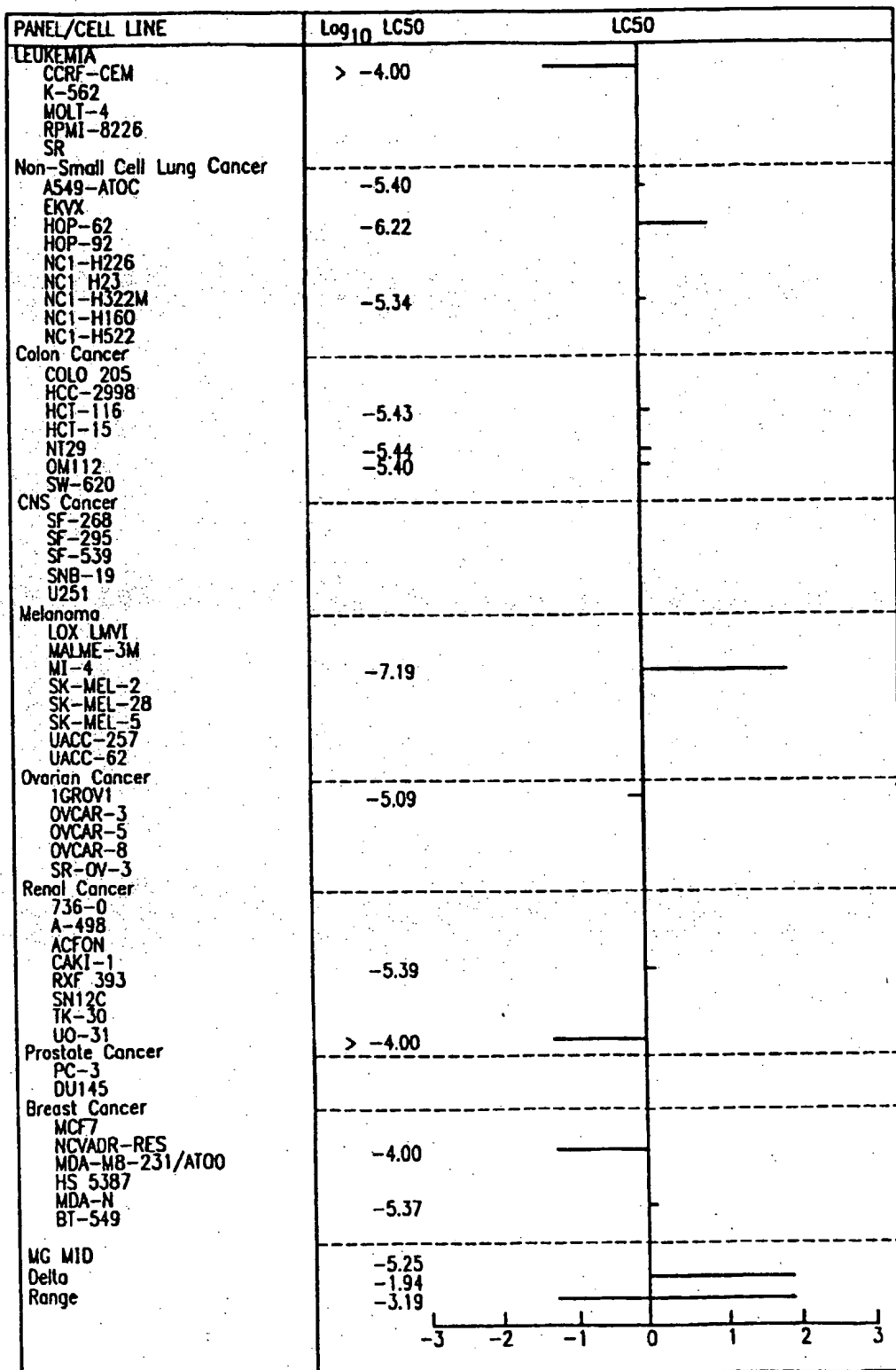


FIG. 57-A

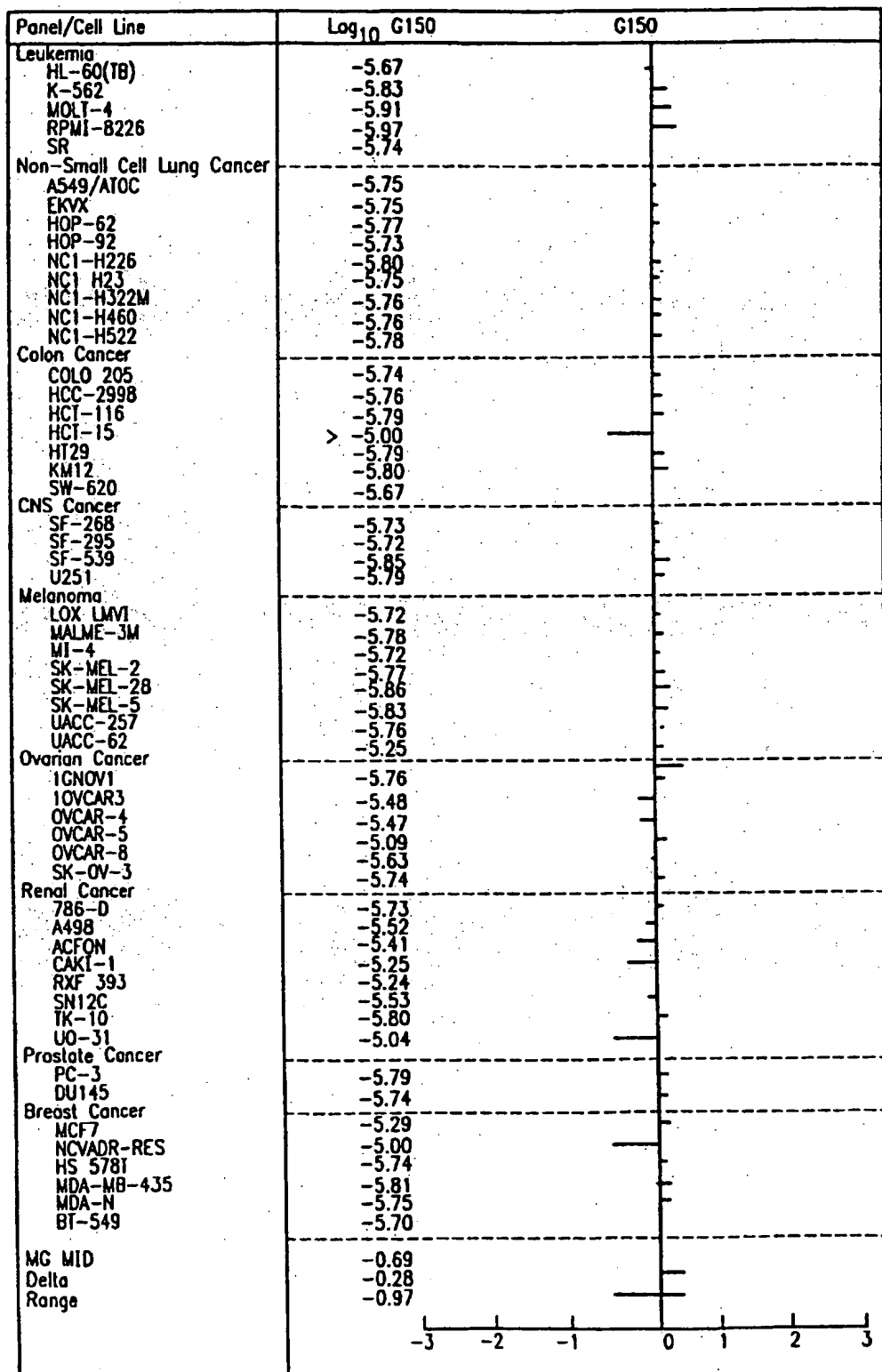


FIG. 57-B

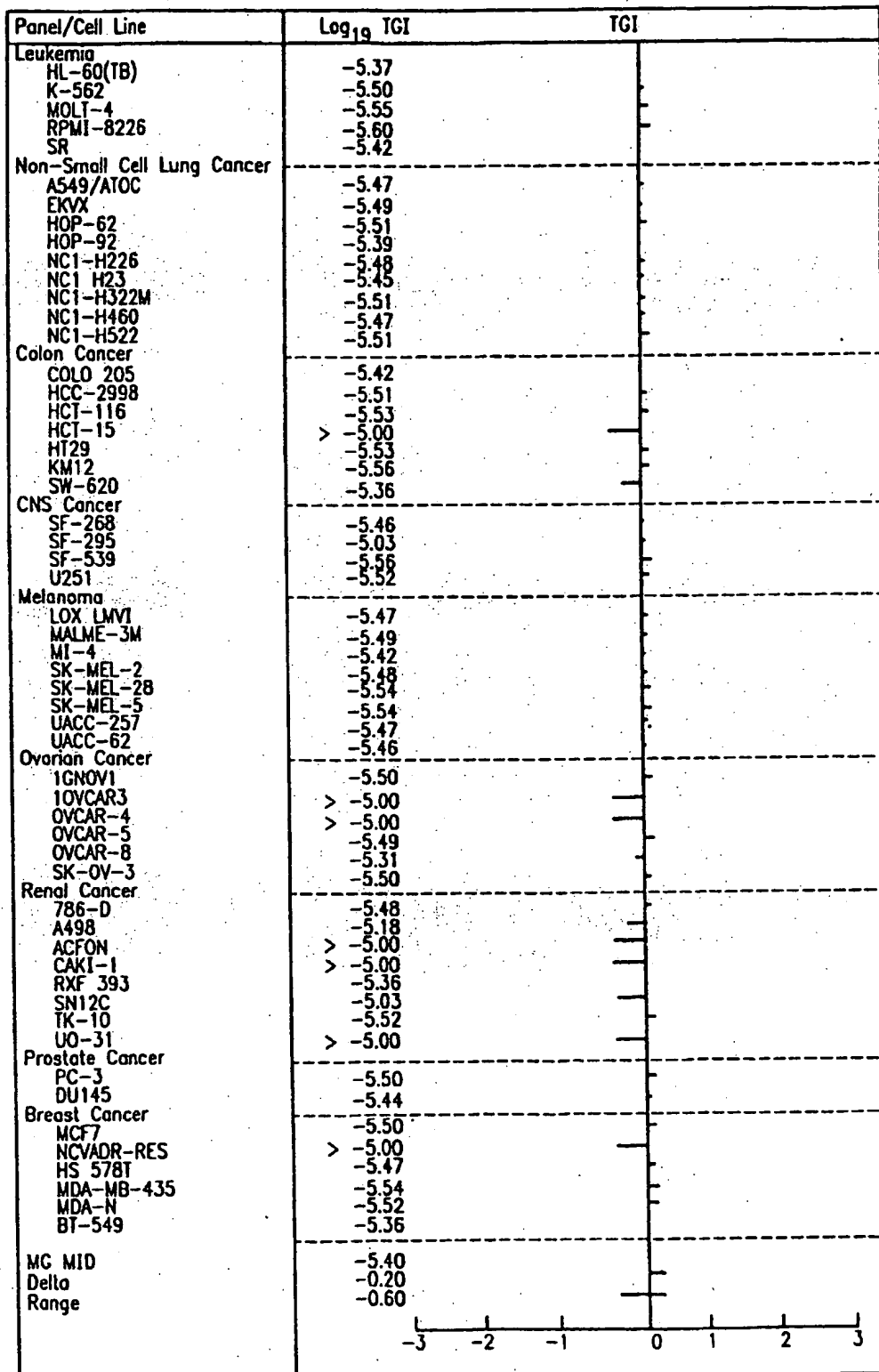


FIG. 57-C

| Panel/Cell Line | Log ₁₀ LC50 | LC50 |
|-----------------------------------|------------------------|------|
| Leukemia | | |
| HL-60(TB) | -5.08 | |
| K-562 | -5.16 | |
| MOLT-4 | -5.19 | |
| RPMI-8226 | -5.22 | |
| SR | -5.31 | |
| Non-Small Cell Lung Cancer | | |
| A549/ATOC | -5.20 | |
| EKVX | -5.22 | |
| HOP-62 | -5.26 | |
| HOP-92 | -5.05 | |
| NCI-H226 | -5.16 | |
| NCI H23 | -5.16 | |
| NCI-H322M | -5.25 | |
| NCI-H460 | -5.19 | |
| NCI-H522 | -5.24 | |
| Colon Cancer | | |
| COLO 205 | -5.30 | |
| HCC-2998 | -5.25 | |
| HCT-116 | -5.26 | |
| HCT-15 | > -5.00 | |
| HT29 | -5.26 | |
| KM12 | -5.27 | |
| SW-620 | > -5.00 | |
| CNS Cancer | | |
| SF-268 | -5.20 | |
| SF-295 | -5.15 | |
| SF-539 | -5.26 | |
| U251 | -5.25 | |
| Melanoma | | |
| LOX LMVI | -5.23 | |
| MALME-3M | -5.20 | |
| MI-4 | -5.12 | |
| SK-MEL-2 | -5.20 | |
| SK-MEL-28 | -5.22 | |
| SK-MEL-5 | -5.25 | |
| UACC-257 | -5.18 | |
| UACC-62 | -5.16 | |
| Ovarian Cancer | | |
| IGNOV1 | -5.25 | |
| OVCA3 | > -5.00 | |
| OVCA4 | > -5.00 | |
| OVCA5 | -5.20 | |
| OVCA8 | > -5.00 | |
| SK-OV-3 | -5.25 | |
| Renal Cancer | | |
| 786-D | -5.24 | |
| A498 | > -5.00 | |
| ACFON | > -5.00 | |
| CAKI-1 | > -5.00 | |
| RXF 393 | > -5.00 | |
| SN12C | > -5.00 | |
| TK-10 | -5.23 | |
| UO-31 | > -5.00 | |
| Prostate Cancer | | |
| PC-3 | -5.23 | |
| DU145 | -5.14 | |
| Breast Cancer | | |
| MCF7 | -5.23 | |
| NCVADR-RES | > -5.00 | |
| HS 578T | -5.20 | |
| MDA-MB-435 | -5.27 | |
| MDA-N | -5.26 | |
| BT-549 | -5.02 | |
| MG MID | -5.16 | |
| Delta | -0.11 | |
| Range | -0.27 | |

-3 -2 -1 0 1 2 3

FIG. 58-A

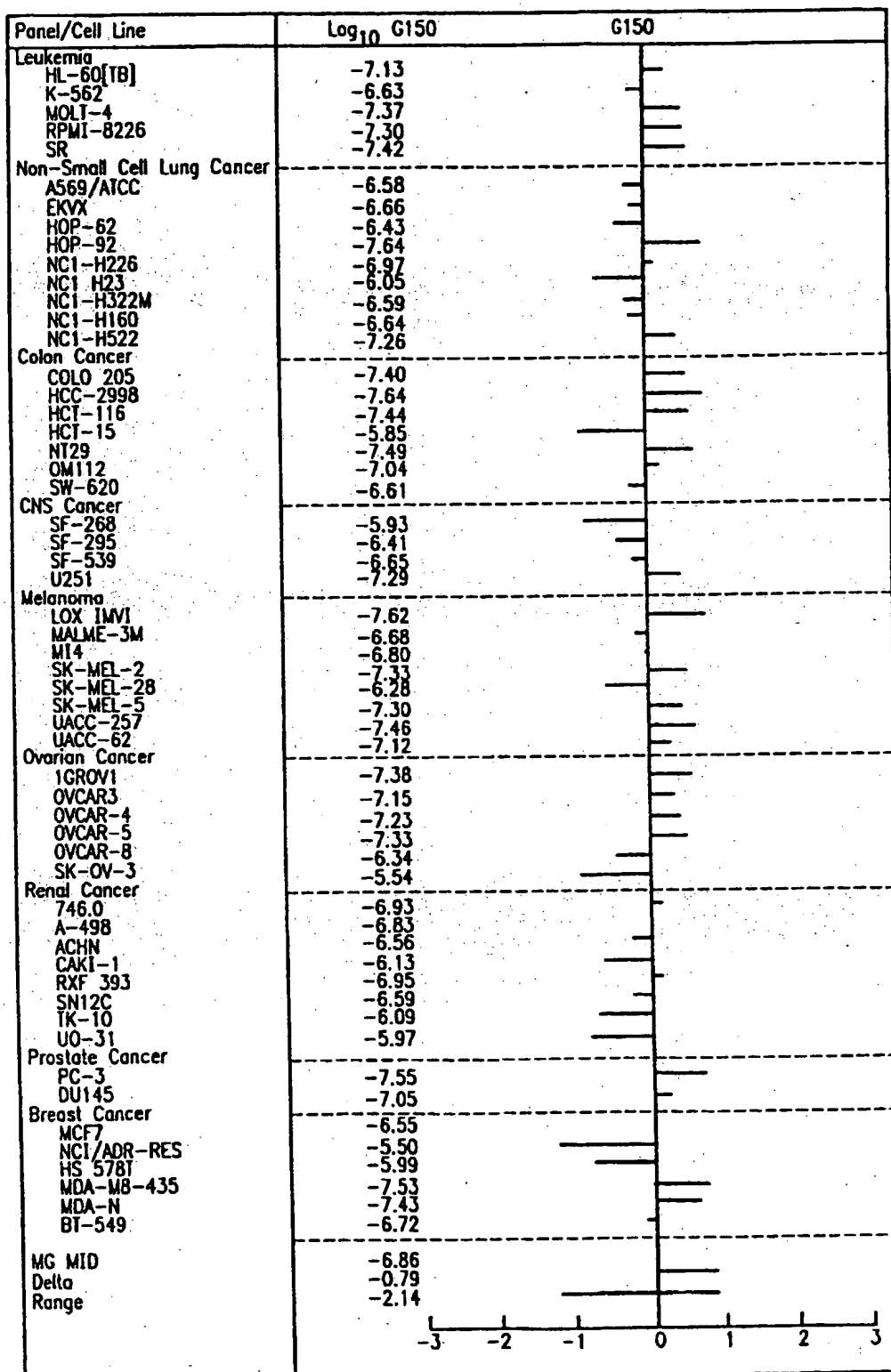


FIG. 58-B

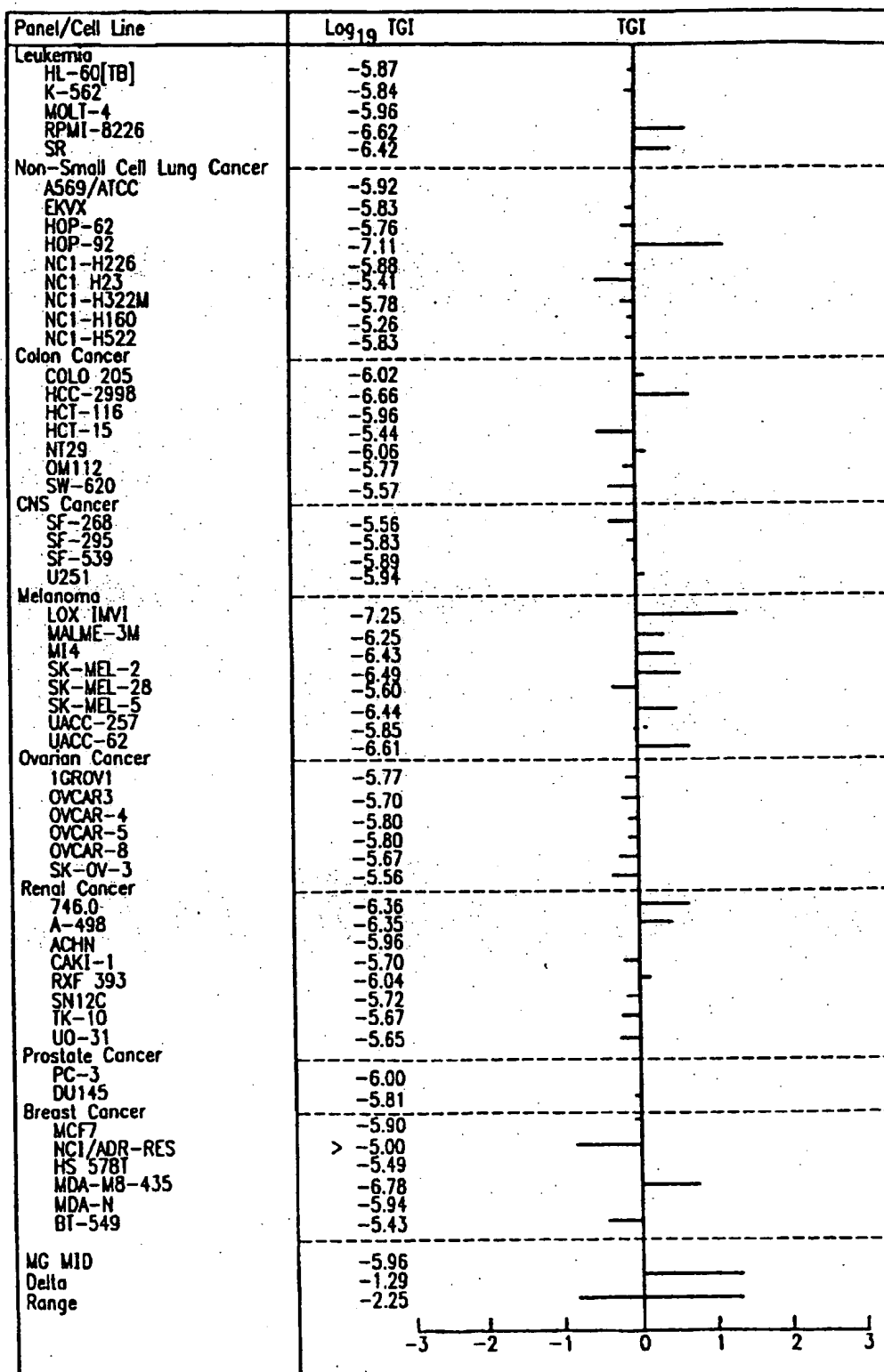


FIG. 58-C

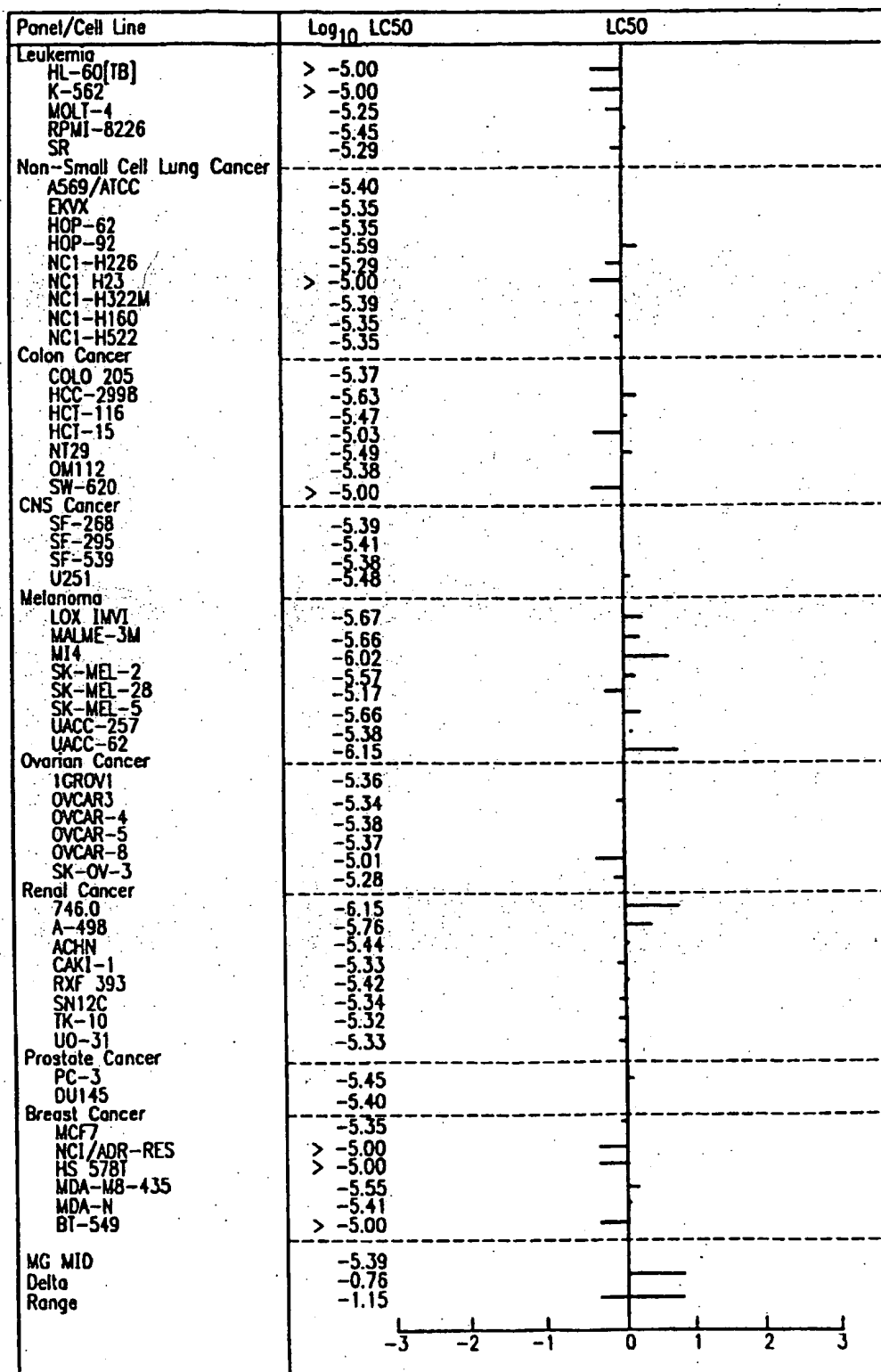


FIG. 59-A

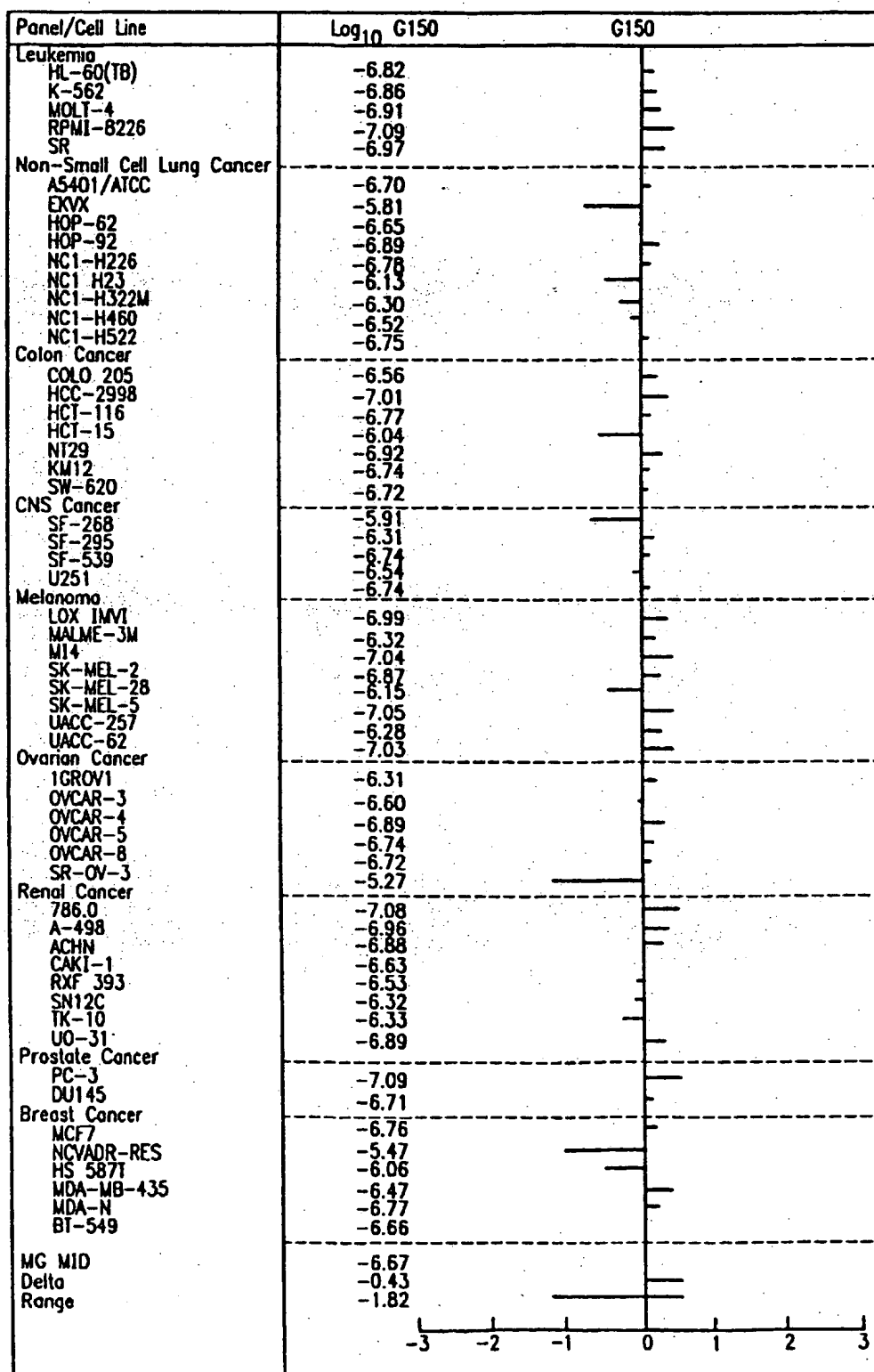


FIG. 59-B

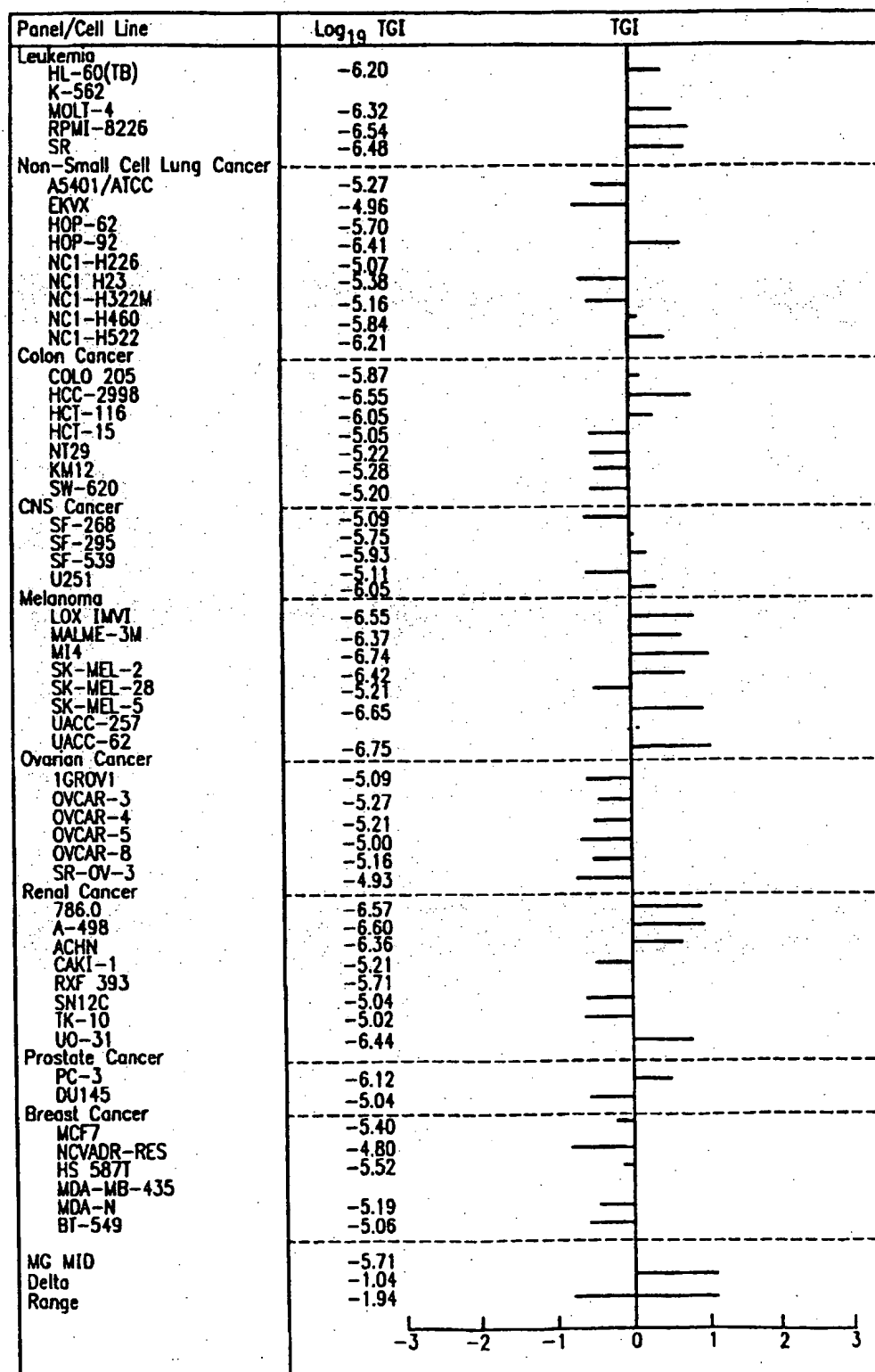


FIG. 59-C

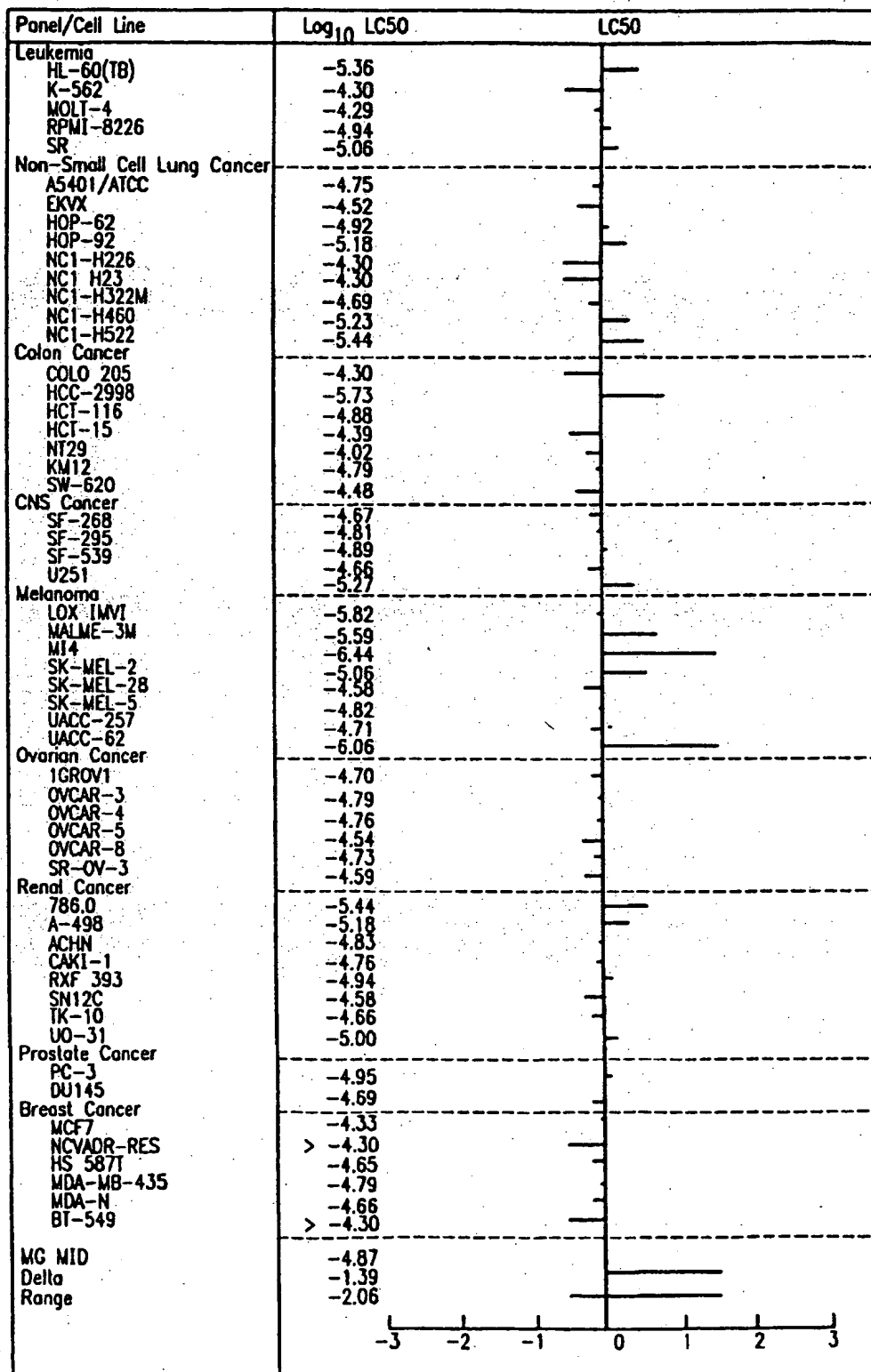


FIG. 60-A

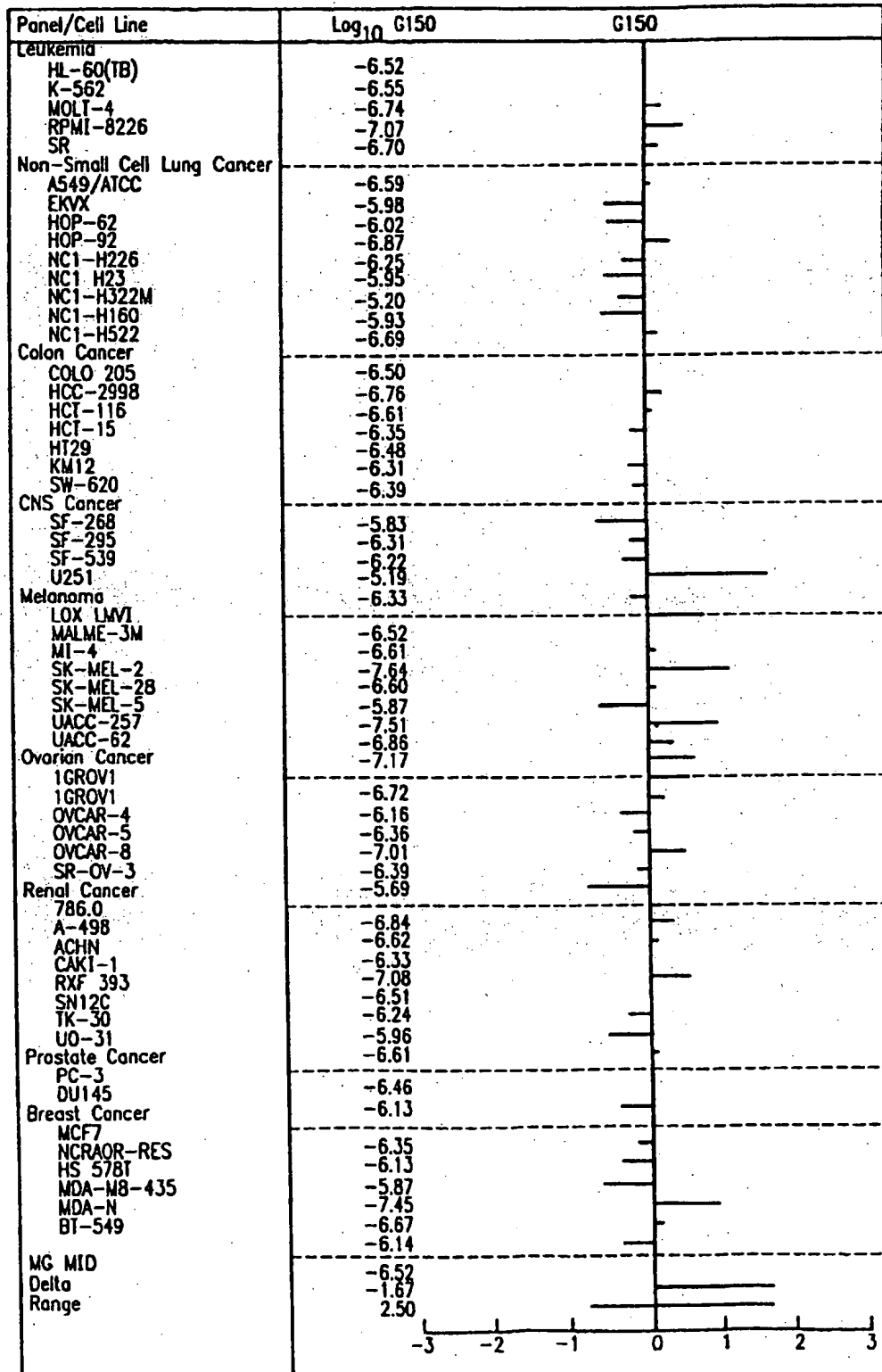


FIG. 60-B

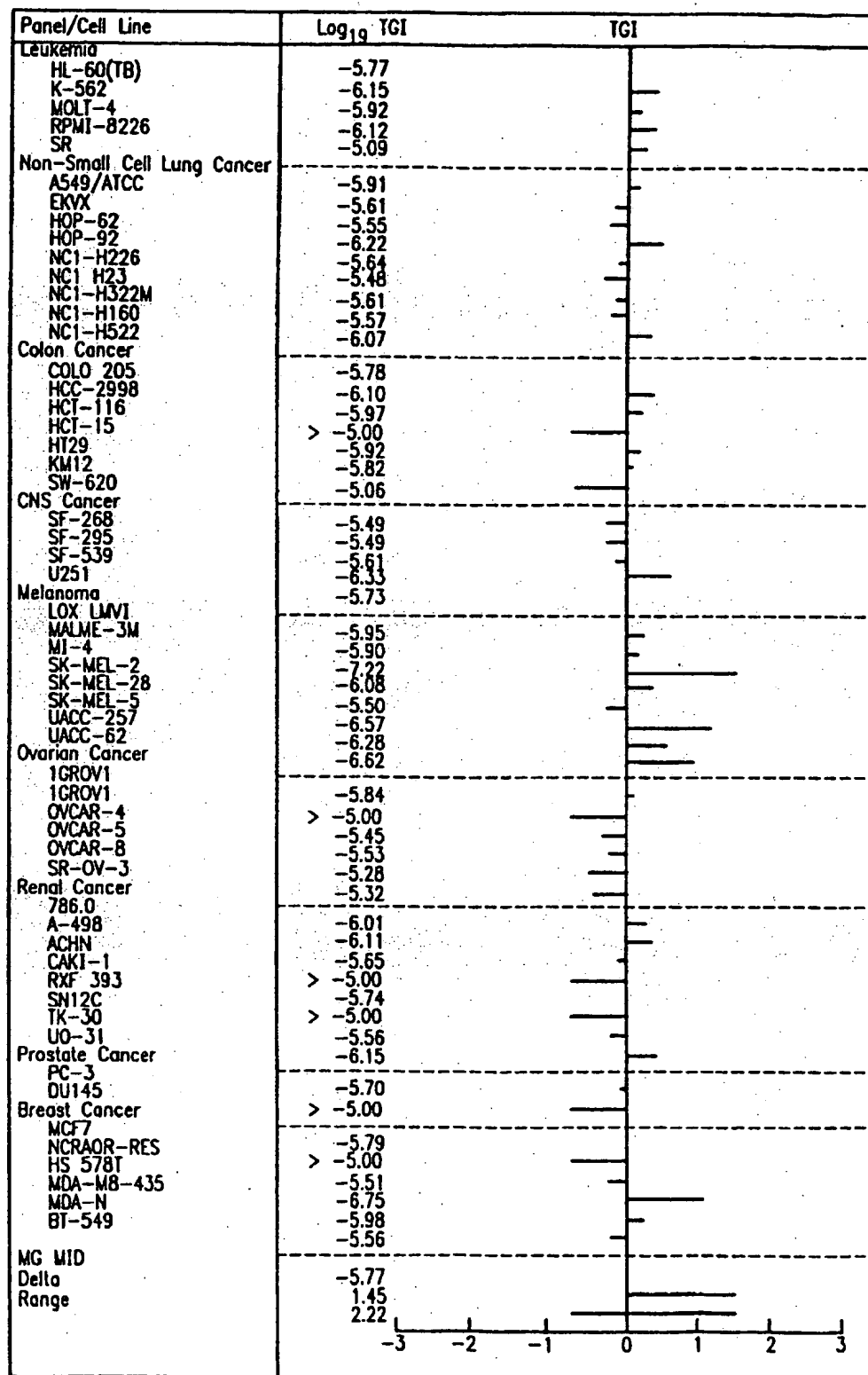


FIG. 60-C

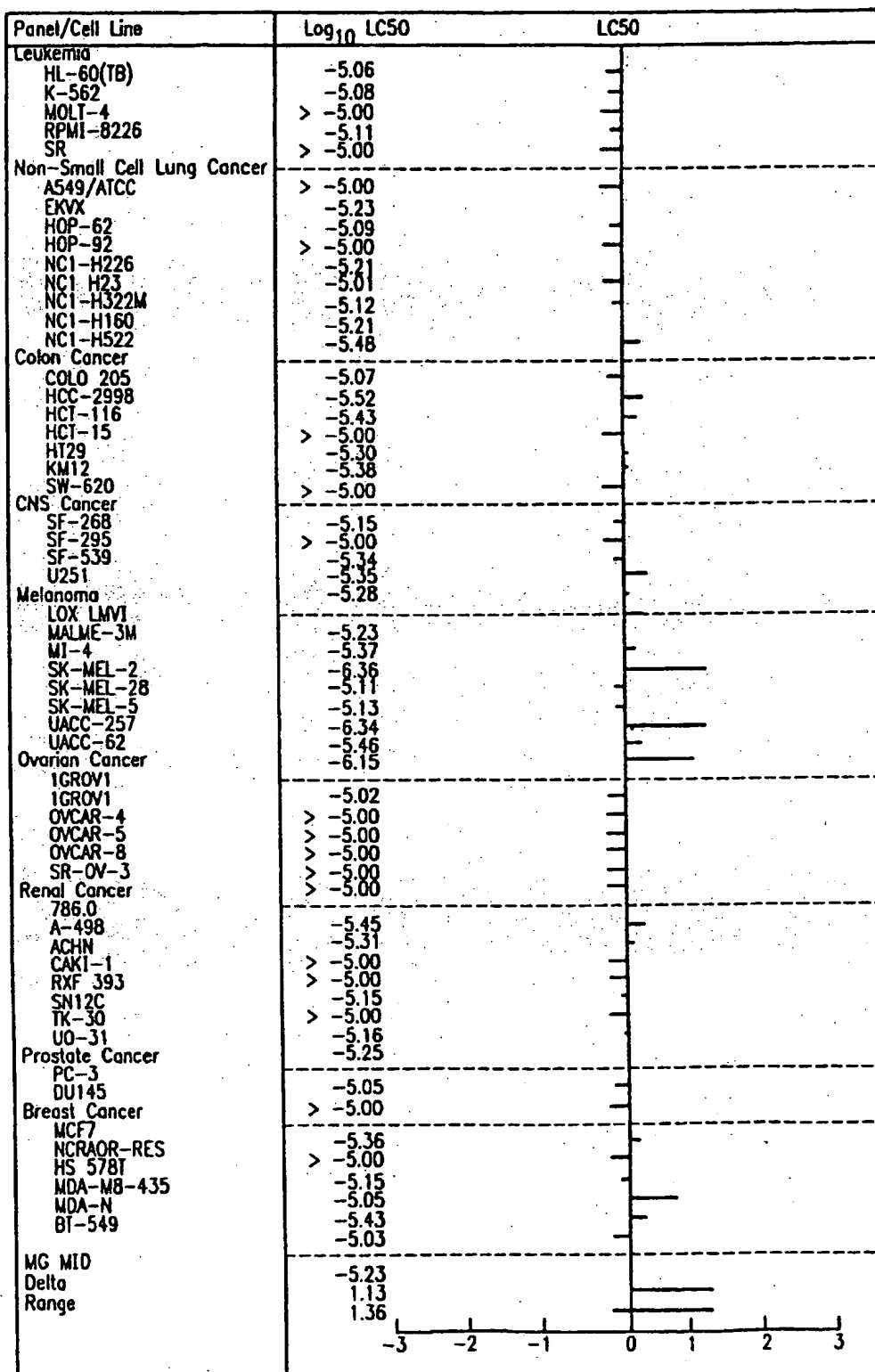


FIG. 61-A

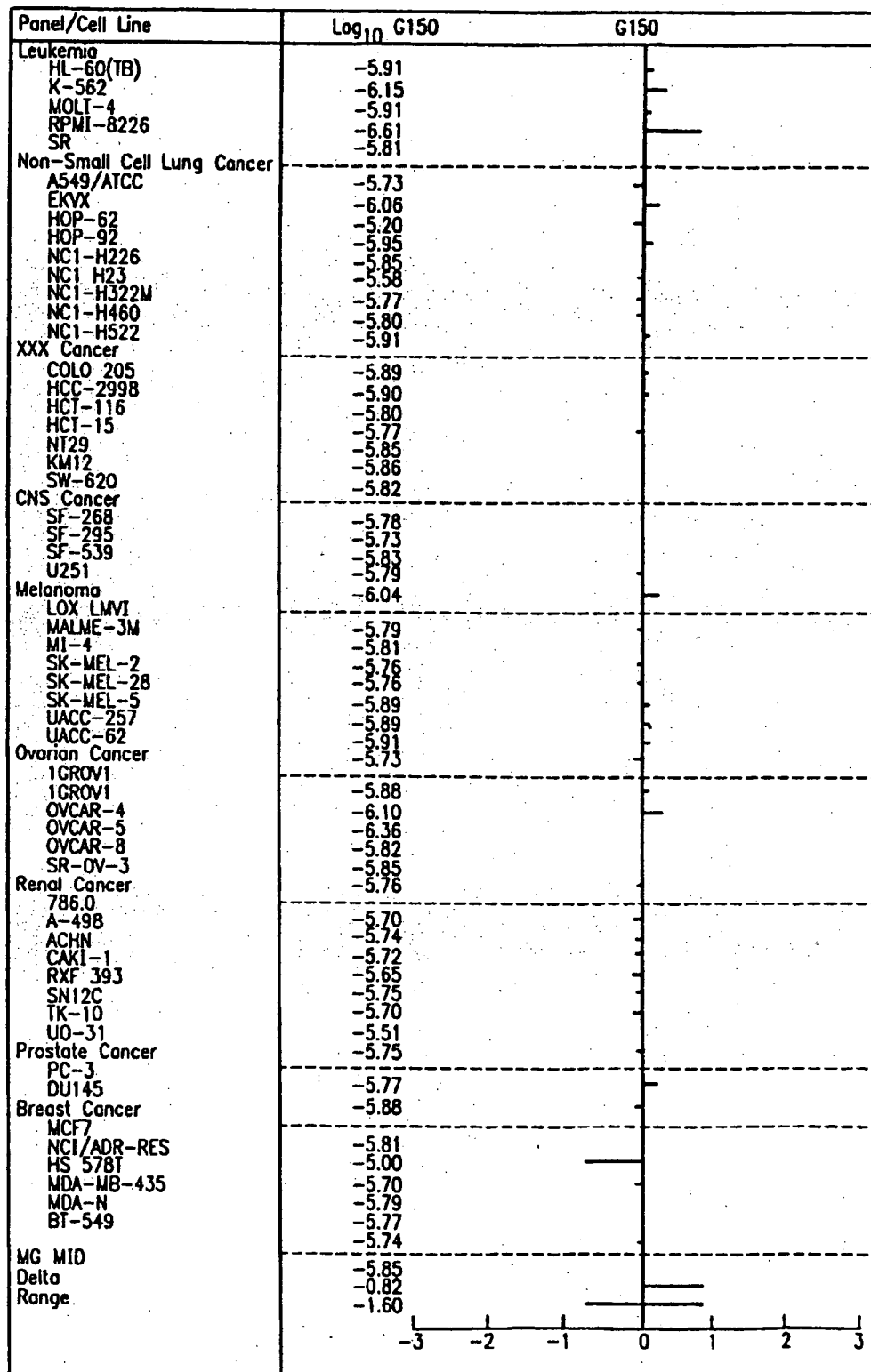


FIG. 61-B

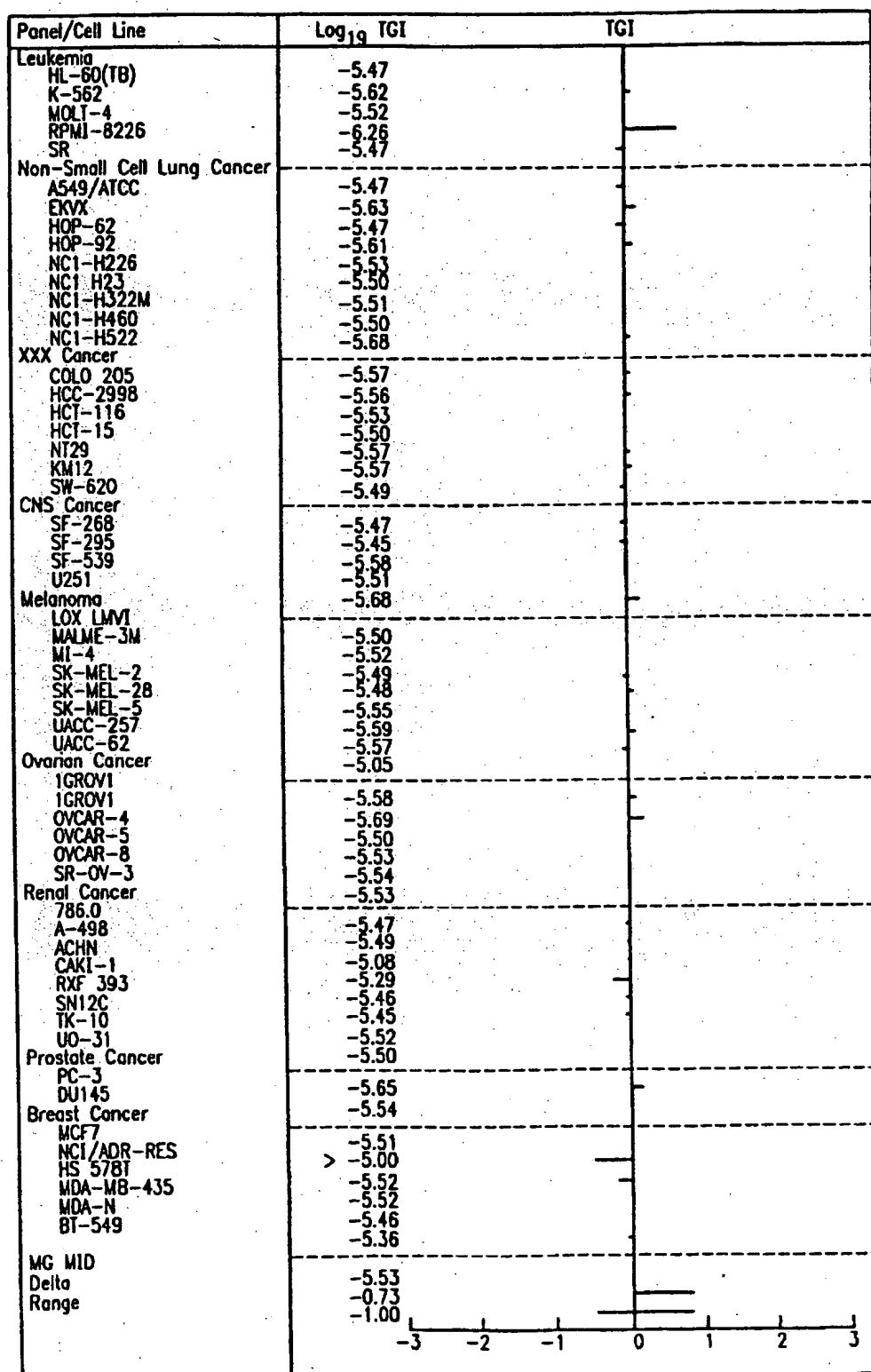


FIG. 61-C

| Panel/Cell Line | Log ₁₀ LC50 | LC50 |
|-----------------------------------|------------------------|------|
| Leukemia | | |
| HL-60(TB) | -5.33 | |
| K-562 | -5.36 | |
| MOLT-4 | -5.14 | |
| RPMI-8226 | -5.34 | |
| SR | -5.10 | |
| Non-Small Cell Lung Cancer | | |
| A549/ATCC | -5.21 | |
| EKVX | -5.33 | |
| HOP-62 | -5.23 | |
| HOP-92 | -5.27 | |
| NCI-H226 | -5.21 | |
| NCI H23 | -5.19 | |
| NCI-H322M | -5.26 | |
| NCI-H460 | -5.18 | |
| NCI-H522 | -5.25 | |
| XXX Cancer | | |
| COLO 205 | -5.25 | |
| HCC-2998 | -5.27 | |
| HCT-116 | -5.27 | |
| HCT-15 | -5.21 | |
| NT29 | -5.23 | |
| KM12 | -5.28 | |
| SW-620 | -5.16 | |
| CNS Cancer | | |
| SF-268 | -5.16 | |
| SF-295 | -5.23 | |
| SF-539 | -5.25 | |
| U251 | -5.24 | |
| Melanoma | | |
| LOX LMVI | -5.33 | |
| MALME-3M | -5.22 | |
| MI-4 | -5.24 | |
| SK-MEL-2 | -5.22 | |
| SK-MEL-28 | -5.19 | |
| SK-MEL-5 | -5.27 | |
| UACC-257 | -5.29 | |
| UACC-62 | -5.24 | |
| Ovarian Cancer | | |
| IGROV1 | -5.18 | |
| IGROV1 | -5.27 | |
| OVCAR-4 | -5.35 | |
| OVCAR-5 | -5.15 | |
| OVCAR-8 | -5.24 | |
| SR-OV-3 | -5.22 | |
| Renal Cancer | | |
| 786.0 | -5.25 | |
| A-498 | -5.23 | |
| ACHN | -5.23 | |
| CAKI-1 | -5.24 | |
| RXF 393 | > -5.00 | |
| SN12C | -5.18 | |
| TK-10 | -5.21 | |
| UO-31 | -5.24 | |
| Prostate Cancer | | |
| PC-3 | -5.25 | |
| DU145 | -5.32 | |
| Breast Cancer | | |
| MCF7 | -5.27 | |
| NCI/ADR-RES | -5.21 | |
| HS 578T | > -5.00 | |
| MDA-MB-435 | > -5.00 | |
| MDA-N | -5.26 | |
| BT-549 | -5.26 | |
| MG MID | | |
| Delta | -5.17 | |
| Range | -5.22 | |
| | -0.10 | |
| | -0.39 | |

-3 -2 -1 0 1 2 3

FIG. 62-A

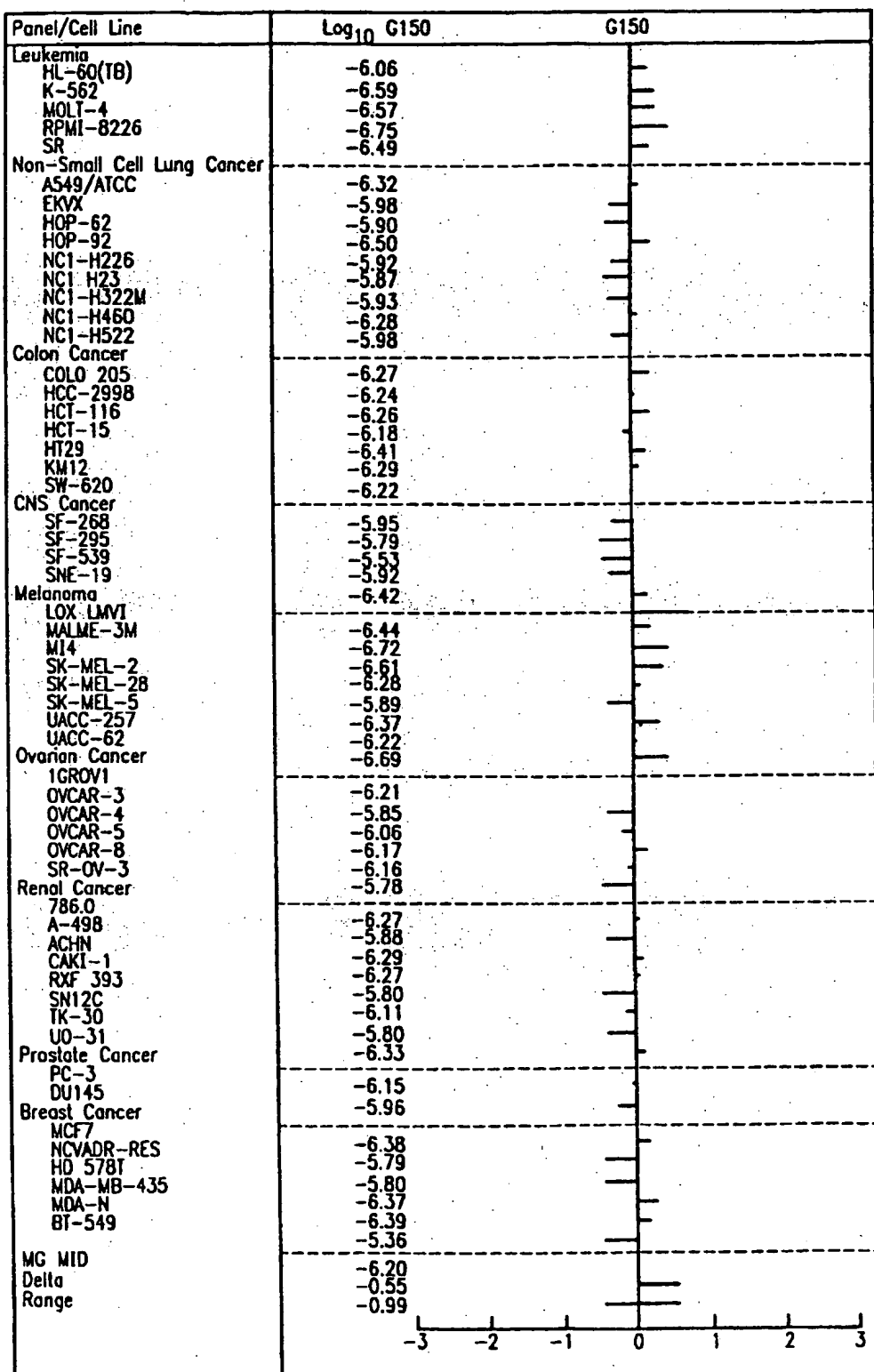


FIG. 62-B

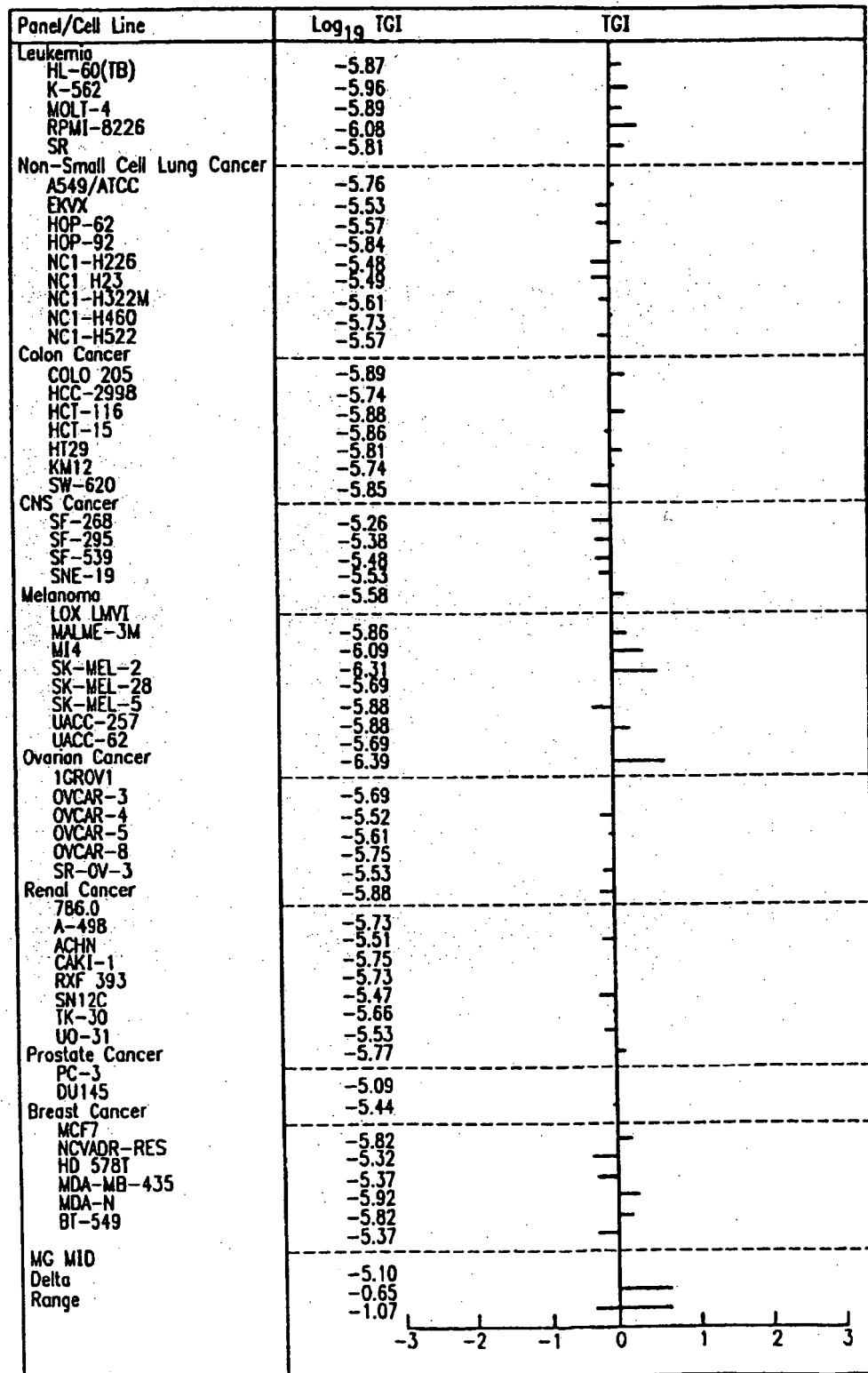


FIG. 62-C

